



6372424

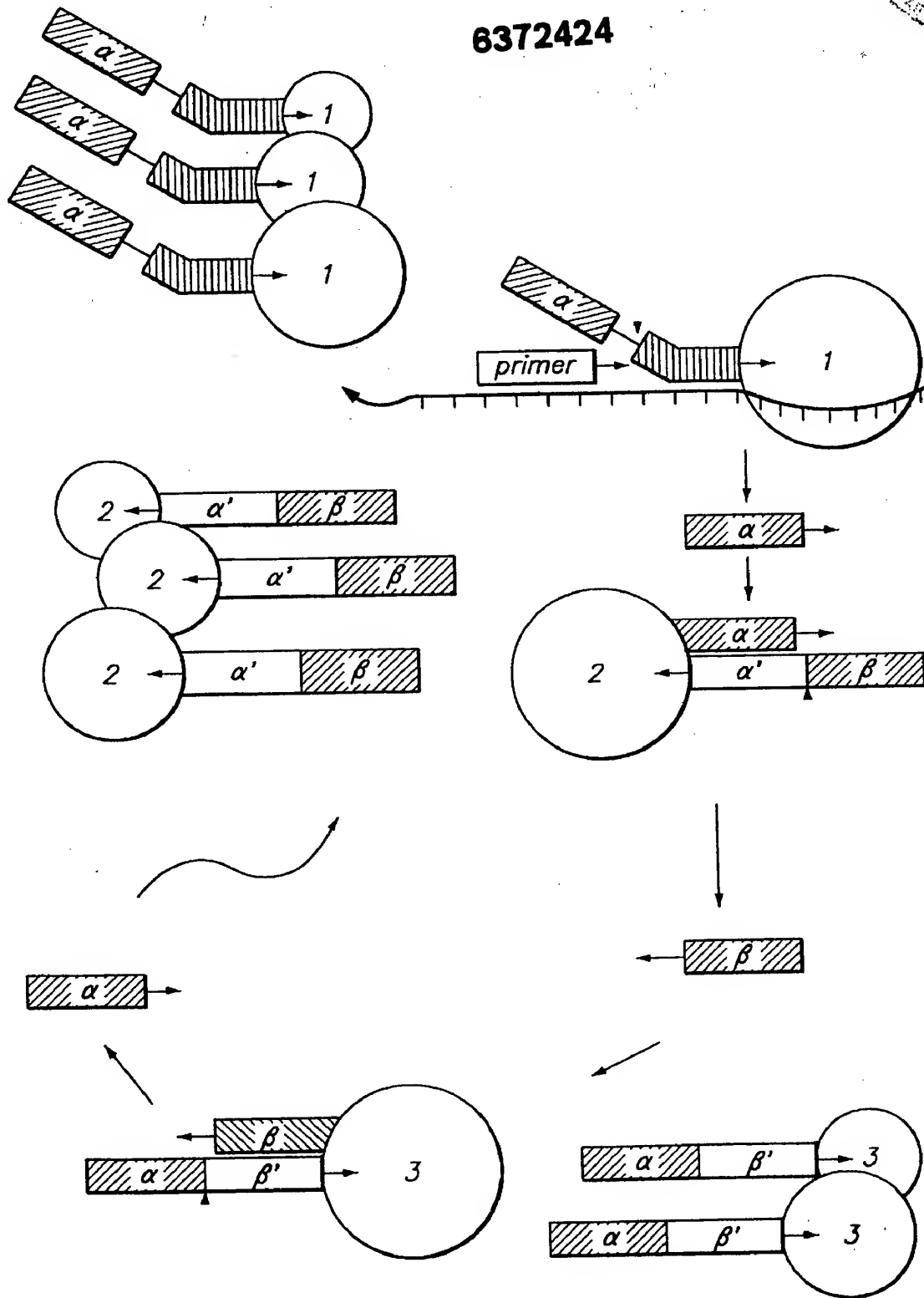


FIG. 1A

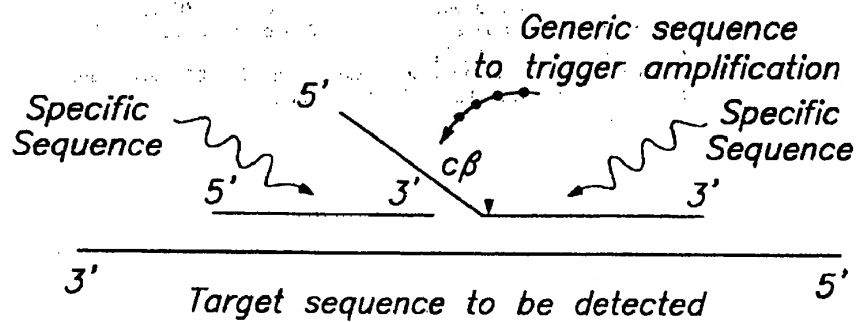


FIG. 1B PART ONE: TRIGGER REACTION

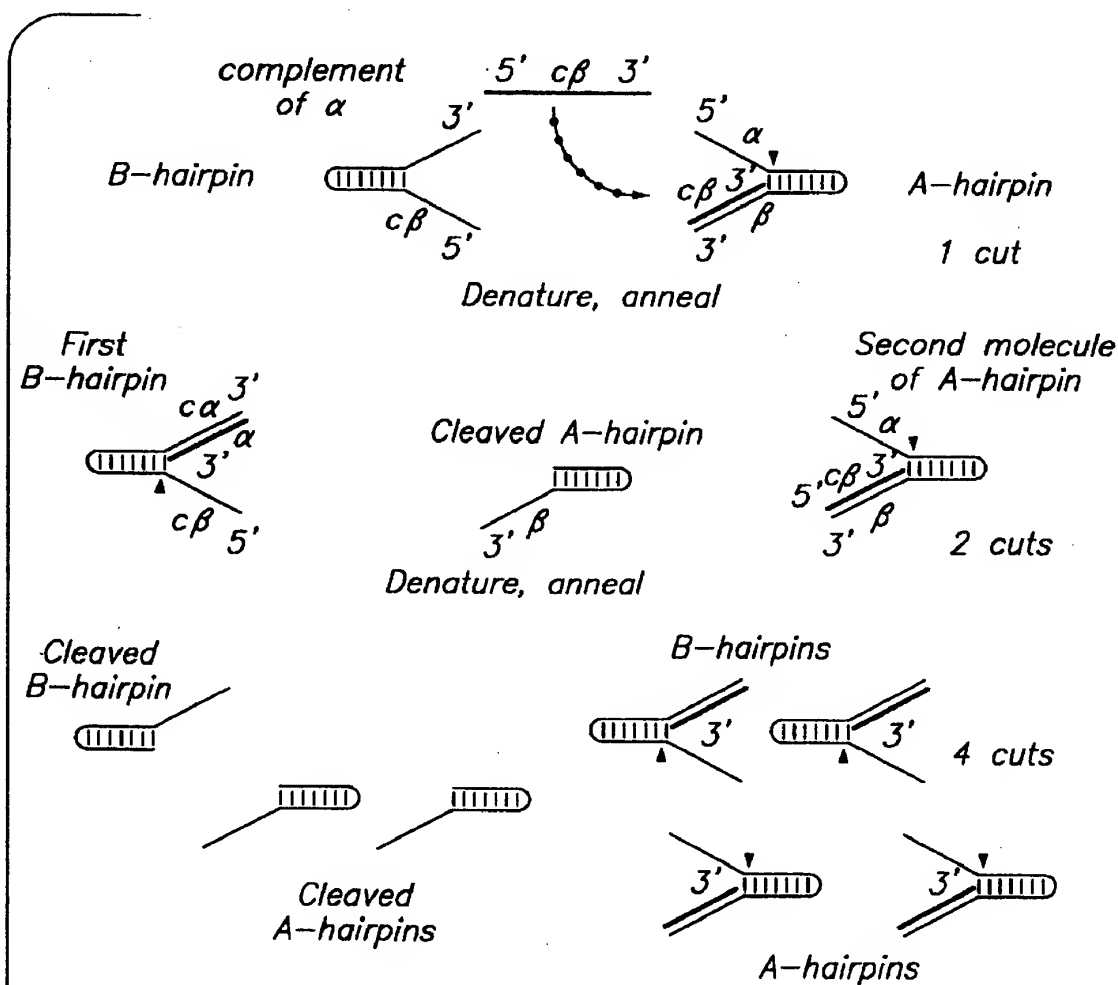


FIG. 1C PART TWO: DETECTION REACTION



FIG. 2A

MAJORITY [SEQ ID NO:7] ATGXXGGCGATGCTTCCCTCTTGAGCCCAAGCCCGGCTCCTCCTGGTGAGCGGCCACCACTGGCT

DNAPTAA [SEQ ID NO:1] ... AG. G. ... G. ... G. ... C. G. ... 70
DNAPTFL [SEQ ID NO:2] ... GA. ... G. ... A. ... 67
DNAPTTH [SEQ ID NO:3] ... GA. ... G. ... A. ... 70

MAJORITY ACCGCACCTTCTGGCCCTGAAGGGCTCACCACGAGCCGGGGGAACGGGTGGAGCGGCTCTACGGCT

DNAPTAA ... CA. ... G. ... G. ... G. ... 140
DNAPTFL ... T. ... C. ... C. ... C. ... 137
DNAPTTH ... G. ... G. ... C. ... T. ... 140

MAJORITY CGCCAGAGGCTCTCTCAAGGCCCTGAAGGAGGACGGGGACXXGGCGGTGXTGGTCTTGAGGCCAAG

DNAPTAA ... G. ... G. ... A. ... 207
DNAPTFL ... A. ... G. ... T. ... 204
DNAPTTH ... T. ... AA. ... C. ... CT. ... 210

MAJORITY GCGCCCTGCTTGGGCGAGGCTACGAAGGCTAGAAGCGGGCGGGCCGCCACCCGGAGGACTTC

DNAPTAA ... G. ... G. ... G. ... 277
DNAPTFL ... GA. ... G. ... C. ... 274
DNAPTTH ... GA. ... G. ... C. ... 280

MAJORITY CCGGCGAGCTCGGCTCATCAAGGAGCTGGTGGACCTCTGGGGCTTGGGGGCTGAGGCTCCCCGGCTA

DNAPTAA ... A. ... G. ... G. ... 347
DNAPTFL ... G. ... T. ... A. ... G. ... 344
DNAPTTH ... T. ... A. ... C. ... 350

FIG. 2B

MAJORITY [SEQ ID NO:73]	CGAGGGGGGACGAGCGTCTGGCCACCCCTGGCCCAAGAGGGGGGAAAGGAGGGGTACGAGGTCGGCATCCGC	
DNAPTAA [SEQ ID NO:13]C.....G.....C.....G.....	417
DNAPTFL [SEQ ID NO:23]	T.....G.....CG.....	414
DNAPTTH [SEQ ID NO:33]T..C.....	420
MAJORITY	ACCGCCGACCGGACCTCTACGAGCTCCTTCCGACCCGATCGCCGTCCTCCACCCCGAGGGGTACCTCA	
DNAPTAAAAA.....T.....CA.....	487
DNAPTFL	..T.....G.....G.....A.....T.....G.....	484
DNAPTTHA..G.C.....G.....CC.....	490
MAJORITY	TCACCCGGGGCTGGCTTGGGAGAACTACGGGCTGAGGGCCGGAGCAGTGGGTGGACTACCGGGCCCTGGC	
DNAPTAAG.....A.....C..C.....CC.....A..	557
DNAPTFLAC.....C.C.....	554
DNAPTTHA.....C.....T..C.....C.T..560	
MAJORITY	GGGGGACCCCTCCGACAACTCCCCGGGCTCAAGGGCATCGGGGGAGAGACCGCCCGGAGGCTCCTCXAG	
DNAPTAA	C.....GAG.....T.....G..GAG.....T..GG..	627
DNAPTFLG..T..A.....G.....A..G....A..GGC	624
DNAPTTHTC.....A..	630
MAJORITY	GAGTGGGGGAGCCCTGGAAAAGCTCGTCAAGAACTGGACCGGGGTGAAGCCCGC...CXTCGGGGGAGAGA	
DNAPTAAGC.....C.....A.....	684
DNAPTFLT..C..C.....A.....T...T..G.....C	691
DNAPTTHA.....A.....A.AAA..C.....	700



MAJORITY [SEQ ID NO:7] TCGAGGCCACATGGAXGACCTGAXGCTCTCCCTGGAGGTXTCGACGGAGCCTGCCCGTGG

DNAPTAG	[SEQ ID NO:1]
DNAPTFL	[SEQ ID NO:2]
DNAPTTH	[SEQ ID NO:3]

[S\$O ID NO:1]	T	G	T	A	G	GG	A	764
[S\$O ID NO:2]	GGG	G	C	GGC	T	C	A	761
[S\$O ID NO:3]	A	C	A	C	T	C	G	770

MAJORITY

CGTGGAGCTTCGGCGAAGXGGCGGCGACCGCGAAGCGCTTAAGGCCCTTCTCGAGAGCGCTCGAGTTT

DNAPIAQ
DNAPIFL
DNAPITB

.....	A.	T.	C.	I.	831
.....	A.	T.	C.	I.	834
.....	A.	T.	C.	I.	831
.....	A.	T.	C.	I.	840

MAJORITY

GGAGGCTCCTCCACGAGTTCGGCCCTCCTGGAGGGCCCAAGGCCCTGGAGGAGGCCCTGCCCGCCG

DNAPTAD
DNAPTFL
DNAPTTH

.....T.....904
AA.....901
G.....910
G.....910
G.....910

MAJORITY

CGGAAGGGCCCTTCGTGGGCTTGTCCCTTCCGGCCCGAGCCGATGTGGCCGAGCTTCTGGCCCTGGC

DNAPTAD
DNAPTFL
DNAPTIN

.....	AAG.....	974
.....	G.....	975
T.....	T.....	976
.....	TC.....	977
.....	978
.....	979
.....	980
.....	981
.....	982
.....	983
.....	984
.....	985
.....	986
.....	987
.....	988
.....	989
.....	990
.....	991
.....	992
.....	993
.....	994
.....	995
.....	996
.....	997
.....	998
.....	999
.....	1000

MAJORITY

CGCGGCGAGGGGCGGGGTCCAGCGGGGCAAGAGACCCCTTAXGGGCTXAGGGACCTXAAGGAGGTG

DNAPTAD
DNAPTFL
DNAPTTH

.....	G	C. C. G.	T. A.	AA. C.	G.	G.	1044
T. GG. GT	G. GG.	T.	A.	C.	G.	T.	1041
TC	C	C	GG	R	A	A	1050

FIG. 2D

MAJORITY [SEQ ID NO:7]	GGGGGCTCCTCGCGAAGGACCTGGCCGTTTGGCCCTGAGGAGGGGCTXGACCTCTGCCCGGGGACG	
DNAPTAD [SEQ ID NO:1]G..T.....A.....AG.....C.....A.....T..G.....CC.....C.....	1114
DNAPTFL [SEQ ID NO:2]AA.....G.....G.....C.....G.....T..C..A..A.....	1111
DNAPTTH [SEQ ID NO:3]C.....C.....C.....TC.....G..A.....G.....	1120
MAJORITY	ACCCGATGCTCGCTACCTCCTGGAGCCCTCCAAACACACCCCGAGGGGGTGGCCGGGCTACGG	
DNAPTADT.....	1184
DNAPTFLT.....T.....T.....	1181
DNAPTTHG.....T.....G.....	1190
MAJORITY	GGGGGACTGGACGGAGGAXCGGGGGAGCGGGCCCTGCTXTCGGAGAGGCTCTTCCXGAACCTXXGCGAG	
DNAPTAD	C.....G.....G.....GC.....T.....GCC.....GTG..G..	1254
DNAPTFLT.....A.....GG.....C..C.....A..C...AAA....	1251
DNAPTTHC..C.CCC.C.....C..G.....CAT..G.....CCTTA..	1260
MAJORITY	CGCCTTGAGGGGACGAGAGGCTCCTTTGGCCTTACGAGGAGGTGGAGAGCCGCTTTCGGCGGTCCTGG	
DNAPTAD	A..G.....A.....G.....G.....GCT.....	1324
DNAPTFLA.....A..A..AC.C..C.....G.....G.....GT...	1321
DNAPTTHC.....A.....C.....C.....A.....G.....	1330
MAJORITY	GGCAGATGGAGGCCACGGGGGTXCGGGCTGGAGGTGGCCCTACCTCCAGGGGCTXTCCTGGAGGGTGGCGGA	
DNAPTADG..C.....T...AG...T..G.....C...	1394
DNAPTFL	GG.....C.....C.....T.....C.....A..G	1391
DNAPTTHC.....A.....T.....T.....C.T.....	1400



FIG. 2E

MAJORITY	ESQ ID NO:73	GGAGATCGGCGCCCTCGAGGAGGAGGTCTTCGGCCCTGGCGCGCCGACCCCTTCAAGCTCAAGTCCCGGGAC	
DNAPTAA	[SEQ ID NO:1]GC.....CC.....	1464
DNAPTFL	[SEQ ID NO:2]	...G.G...AG..G.....	1461
DNAPTTH	[SEQ ID NO:3]T.....G.....	1470
MAJORITY		CAGCTGGAAAGGCTGCTCTTGCAGGAGCTXGGGCTTCGGCGCATCGGCAAGACGGAGAAAGACXGGCAAGC	
DNAPTAA	C.....A.....	1534
DNAPTFL	GC.....G.C.G.T.....	1531
DNAPTTH	TA.....T.G.G.....C.A.....A.....	1540
MAJORITY		GCTCCAGCAGCGCGCGCTGCTGGAGGGCCCTXCGXGAGGGCCACCCCATCCTGGAGAAGATCCTGCAGTA	
DNAPTAA	C.....C.C.....	1604
DNAPTFL	T.....G.A.....CCGC.....	1601
DNAPTTH	G.....A.G.....C.....C.....C.....	1610
MAJORITY		CGGGAGGCTCAGCAAGGCTCAAGAACACGCTACATXGACCCGCTGCCXGXGCTCGTCCAGCCGAGGACGGGGC	
DNAPTAA	G.....G.....T.....T.....G.A....A.....	1674
DNAPTFL	A.....C.C...G.....A...C...C...	1671
DNAPTTH	G.G.....C.AAG.....G.....	1680
MAJORITY		CGGCTCCAGACCGCGCTTCAACGAGACGGCCAGCGGGCCAGGGCTTAGTAGCTCCGACCCCAACCTGC	
DNAPTAA	A.....T.....C.....	1744
DNAPTFL	G.....TCC.....	1741
DNAPTTH	G.....	1750

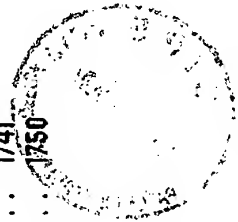


FIG. 2F

MAJORITY [SEQ ID NO:7]	AGAACATCGCCGCTCCGCCACCCXCTGGGGCAGAGGATCCGCCCGGGCCTTCGTGGCCGAGGAGGCTGGGT	
DNAPTAQ [SEQ ID NO:1]G..T..G.....A.C.....G...C.	1814
DNAPTFL [SEQ ID NO:2]G.....T.....C.C.....A.....C.....	1811
DNAPTTH [SEQ ID NO:3]CT.....G.....C...T....C	1820
MAJORITY	GTGGTGGCCCTGGACTATAGCCAGATAGAGCTCGGGGTCTGGCCACCTCTCGGGGGAGGAGAACCTG	
DNAPTAQ	A.....T.T.....C.....A.....G.....C.....	1884
DNAPTFLT.T.....C.....T.....T.....	1881
DNAPTTHC.....C.....C.....A.....	1890
MAJORITY	ATCCGGGCTCTTCCAGAGGGGAGGGACATCCACACCCAGACCGCCAGCTGGATGTTGGGGCTCCCGCCGG	
DNAPTAQC.....GG.....G..	1954
DNAPTFLT.....T.....T.....	1951
DNAPTTHA.....A.....	1960
MAJORITY	AGGCCGTGGACCCCTGATCGCCCGGGGGCCCAAGACCATCAACTTCGGGGCTCCTCTACGGGCATGTCGGG	
DNAPTAQG..	2024
DNAPTFL	A.GG..A.....T.....G.....	2021
DNAPTTHGG.G.....C.....	2030
MAJORITY	CCACGGGCTCTCGCAGGAGCTTGGCATCGGCTACGAGGAGGGGTGGCCTTCATTGAGGGCTACTTCCAG	
DNAPTAQA.....T.....CCA.....T...	2094
DNAPTFLGG.....T.....	2091
DNAPTTH	...T.A.G.....T.A.....A	2100



FIG. 2G

MAJORITY [SEQ ID NO:7] AGCTTCCGCAAGGTGGGGCCCTGGATTGAGAAAGACCTGGAGGAGGGCCAGGAGGGGGGTACGTGGAGA

DNAPTAQ [SEQ ID NO:1]
DNAPTFL [SEQ ID NO:2]
DNAPTTR [SEQ ID NO:3]

.....
A.....GG.....C.....C.CC.....T.....
.....A.....A.....G.....A.....C.....A.....
2164
2161
2170

MAJORITY CCCTCTTCCGGCCGCGGGCGGTAGGTGCCCCGACCTCAACGGCCCGGGTGAAGAGCGTCCGGGAGCGCGGGGGA

DNAPTAQ
DNAPTFL
DNAPTTR

.....C.....A.....AG.G.....C.....
.....T.....C.....
AA.AA.....CA.....C.....
2234
2231
2240

MAJORITY GCGCATGCGCTTCAACATGCCCGTCCAGGGCCACCGCGGACCTCATGAAGCTGGCCATGGTGAAGCTC

DNAPTAQ
DNAPTFL
DNAPTTR

.....
.....G.....T.....
.....CG...T
.....C.....
2304
2301
2310

MAJORITY TTCCGCGCGGTXCAGGAAATGGGGCCAGGATGGTGGTXXCAGGTCCAGGAGGAGCTGGTCCCTCGAGGGCCC

DNAPTAQ
DNAPTFL
DNAPTTR

.....A...GG.....T.....
.....T.....C.....G.....TT.G.....G.....
.....C.C.G...G...C.C.....C.....CC...G.....
2374
2371
2380

MAJORITY CCAAGAGCGCGCGGAGCGGTGGCCGCTTGGCCCAAGGAGGTGATGGAGGGGTCTATCCCCCTGGCGGT

DNAPTAQ
DNAPTFL
DNAPTTR

A.....A.....CC.....CGGC.....G.....
.....G.C.....AG...A.....GG.....CAG..
.....C...C...A...G.....C.....AA..C.....C.....
2444
2441
2450



FIG. 2H

MAJORITY [SEQ ID NO:7]	GGCCCTGGAGGTGGAGGTGGGATGGGGAGGACTGGCTCTCGGCCAAGGAGTAG
DNAPTAA [SEQ ID NO:1]A.....GA
DNAPTFL [SEQ ID NO:2]CG.....
DNAPTTH [SEQ ID NO:3]T.....GT...



FIG. 3A

MAJORITY [SEQ ID NO:8] MXAMLPLFEPKGRVLLVDGHHLAYRTFFALKGLTTSRGEPUQAVYGFAKSLKALKEDG-DAXXUVFDAK

TAO PRO	[SEQ ID NO:4]	RG.....H.....I.....	69
TFL PRO	[SEQ ID NO:5]V.V.....V.V.....	68
TTR PRO	[SEQ ID NO:6]	E.....YK..F.....YK..F.....	70

MAJORITY APSFRHEAYEAYKAGRAPTEDFPROLALIKELVDLLGLXRLEVPGEADDVLTATLAKKAEKEGYEVRIL

TAO PRO	GG.....A.....S.....	139
TFL PROV.....F.....R.....	138
TTR PROFT.....	140

MAJORITY TADRDLYOLLSDRIAVLHPEGYLITPAWLWEKYGLRPEQWVDYRALXGDPSONLPGVKGI GEKTAXKLLX

TAO PRO	K.....H.....D..A.....T..E.....R...E	209
TFL PROE...I.....Y.....A.....I.....QR..IR	208
TTR PROV...V.....H...E.....F...V.....L...K	210

MAJORITY EWGSLNLLKNLDRVKP-XXREKI XAHMEDLXL SXLSXVRTDLPLEVDFAXRREPDRGLRAFLEF

TAO PRO	A.....L...AI...L...D..K..WD..AK.....K.....R.....	278
TFL PROFOH..O...SL...LQ.G..A.A..RK..O.H.....GR..T.NL.....	277
TTR PROENV.....K..L...R..LE..R.....L.QG.....	280

MAJORITY GSLLHEFGLLEXPKALEEAPWPPPEGAFVGVLSRPEPMWAE LLALAAARXGRVHRAXDPLXGLRDLKEV

TAO PRO	S.....K.....D.....G.....PE.YKA.....A	348
TFL PROG...A.....L..SF.....G.WE..L...D...R.....G.	347
TTR PROA.AP.....K.....C.D.....A...A..K.....	350



FIG. 3B

MAJORITY	[SEQ ID NO: 8]	RGLLAKOLAVLALREGLDIXPGDDPMLLAYLLDPSNTTPEGVARRYGGWTE DAGERALLSERLFXNLXX	
TAQ PRO	[SEQ ID NO: 4]	S.....G.P.....E.....A.....A.....WG	418
TFL PRO	[SEQ ID NO: 5]	I.....F.E.....A.....OT.KE	417
TTH PRO	[SEQ ID NO: 6]	S.....V.....AH.....HR..LK	420
MAJORITY RLEGEERLLWLYXEVEKPLSRVLAHMEATGVRLODVAYLOALSLEVAEEI RRLEEEVFRLAGHPFNLNSRD			
TAQ PRO		R...R...A.....R.....A.....A.....	488
TFL PRO		K.....E.....R.....EA.V.Q.....	487
TTH PRO		K.....H.....L.....	490
MAJORITY QLERVLFDELGLPAIGKTEKTKGRSTSAAVLEALREAHPIVEKI LOYRELTKLKNTYIDPLPXLVHPRTG			
TAQ PRO	S.....D.I.....	558
TFL PRO	DR.....A.....K..	557
TTH PRO		R...L...Q.....H.....V.....S.....	560
MAJORITY RLHTRFNOTATATGRLLSSDDPNLONI PVRTPLGORIRRAFVAEEGWXLVALDYSOIELRVLAHLSODENL			
TAQ PRO	I.....L.....	628
TFL PRO	V...V.....	627
TTH PRO	A...A.....	630
MAJORITY IRVFQEGRDIHTQTASWMFGUPPEAVOPLMRRAAKTINFGVLYGMSAHLRSOELAI PYEEAVAFIERYFO			
TAQ PRO		E.....R.....Q.....	698
TFL PRO		S...G.....G...S.....	697
TTH PRO		K.....V.....	700



FIG. 3C

MAJORITY [SEQ ID NO: 8] SFPKVRAWI EKTLEECRRRGYVETLFGRRRYVPDLNARVKSUREAAERMAFNMPVQGTAAOLMKLAMVKL

TAQ PRO [SEQ ID NO: 4]E.....	768
TFL PRO [SEQ ID NO: 5]	Y.....G.....	767
TTH PRO [SEQ ID NO: 6]K.....	770

MAJORITY FPRLEXMGARMLQVHDELVLLEAPKXRAEXVAALAKEVMEGVYPLAVPLEVEVGXGEDWLSAKEX

TAQ PROE.....	833
TFL PROO.L.....	831
TTH PROR.....	835



Genes for Wild-Type and Pol(-)DNAPTaq

Domain

Coding Regions: 5' Nuclease

Polymerase

FIG. 4A

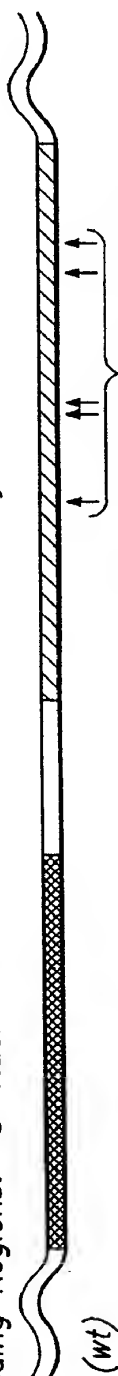


FIG. 4B



FIG. 4C



FIG. 4D



FIG. 4E



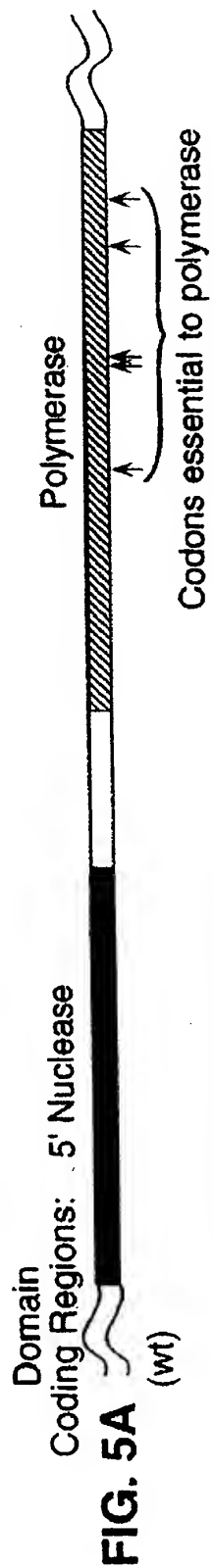
FIG. 4F



FIG. 4G



Genes for Wild-Type and Pol(-) DNAPTfl



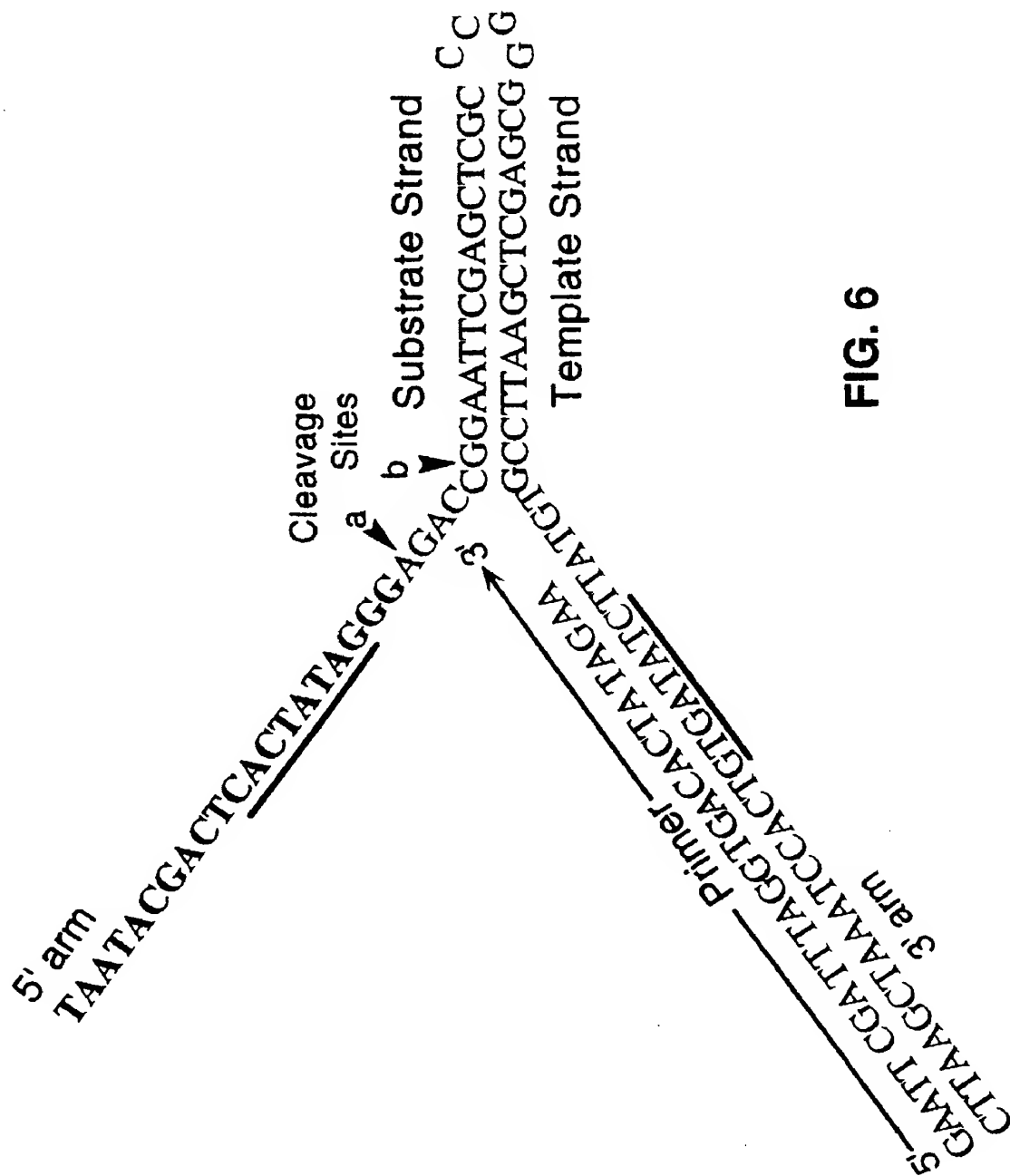


FIG. 6

DNAP
TARGET
DNA

	T		S		
	-	+	-	+	
M					M



FIG. 7

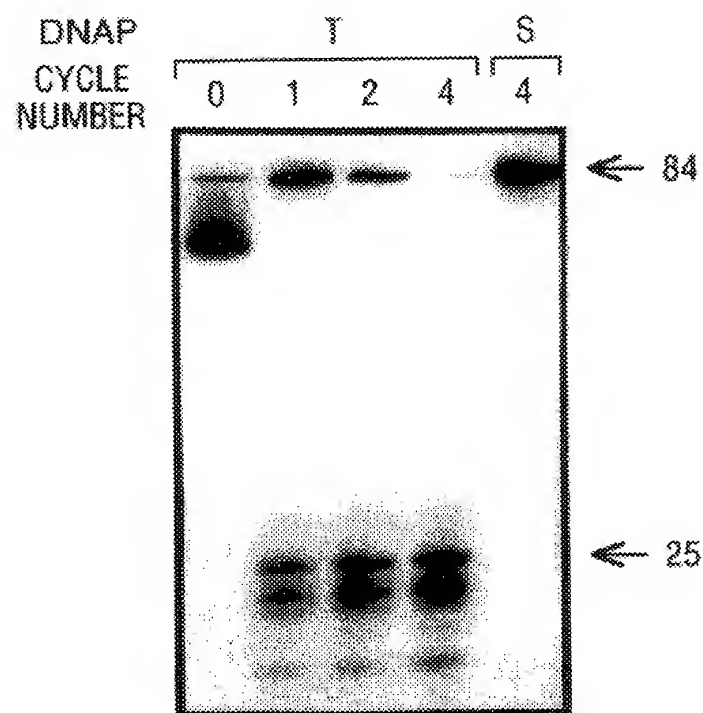


FIG. 8

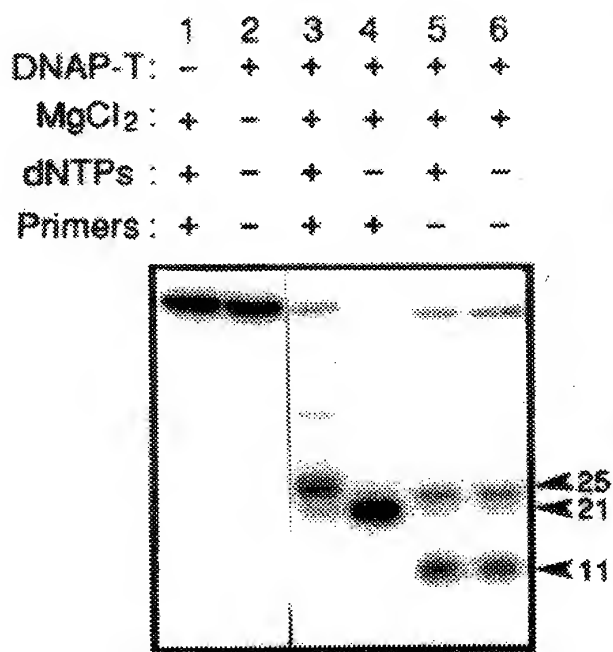


FIG. 9A

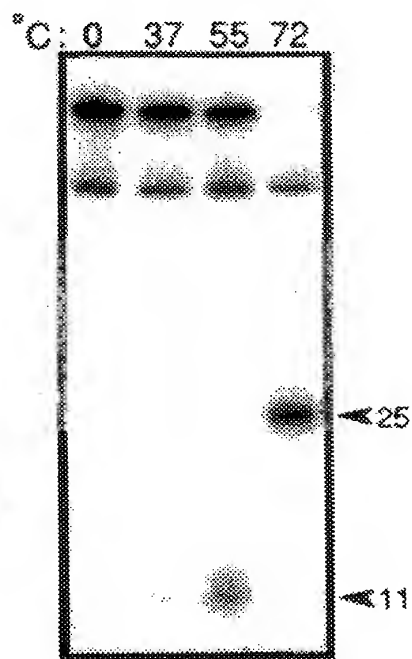


FIG. 9B

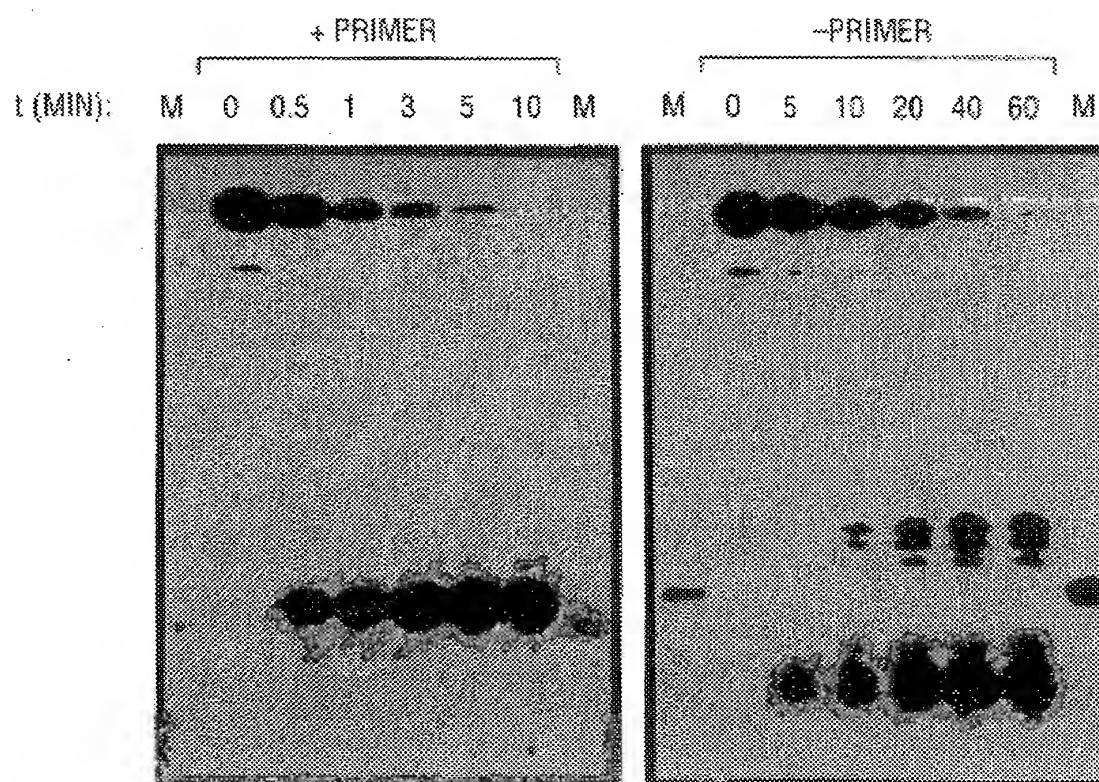
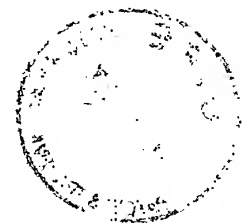
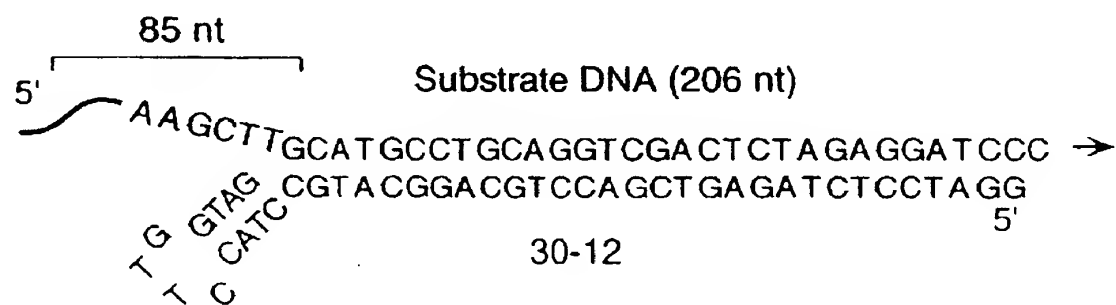
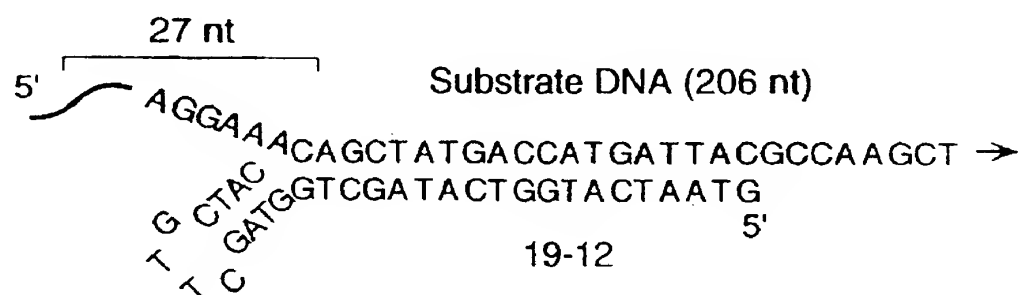


FIG. 10A

FIG. 10B



FIG. 12A



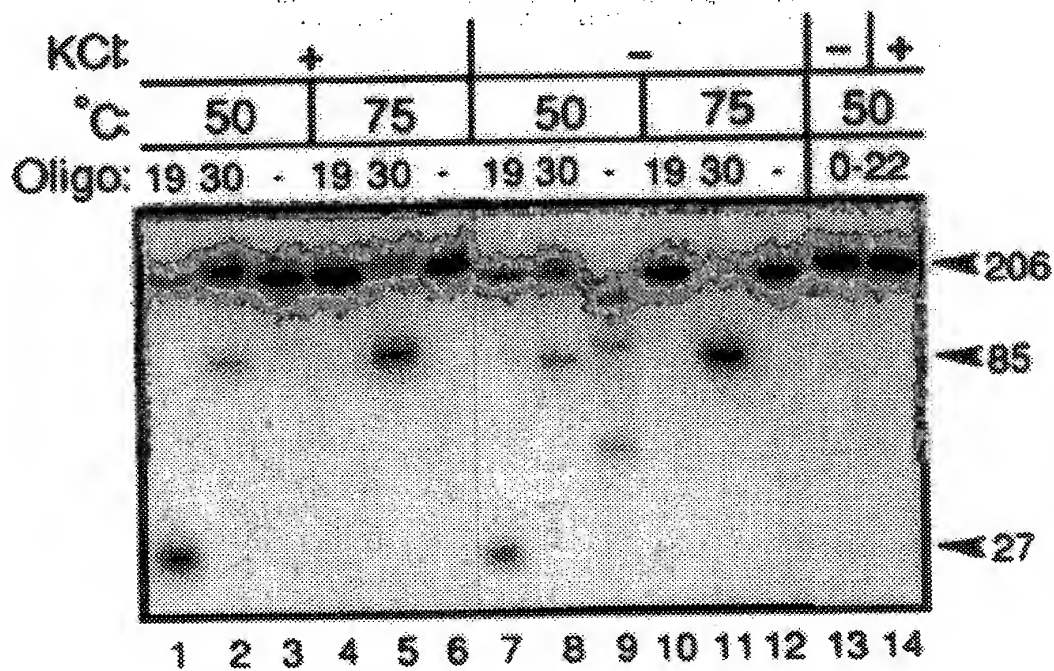


FIG. 12B

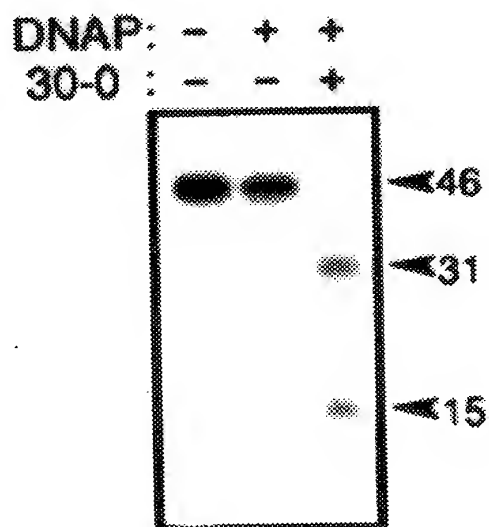


FIG. 13B

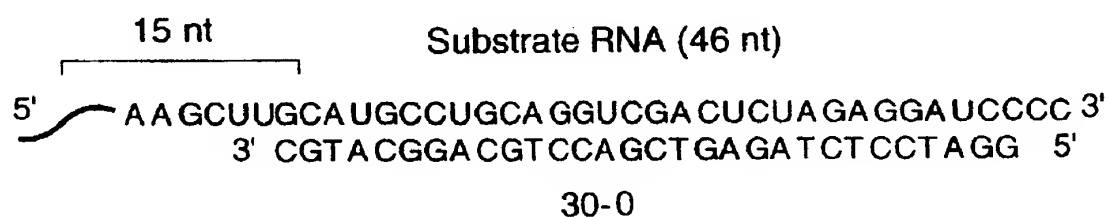


FIG. 13A

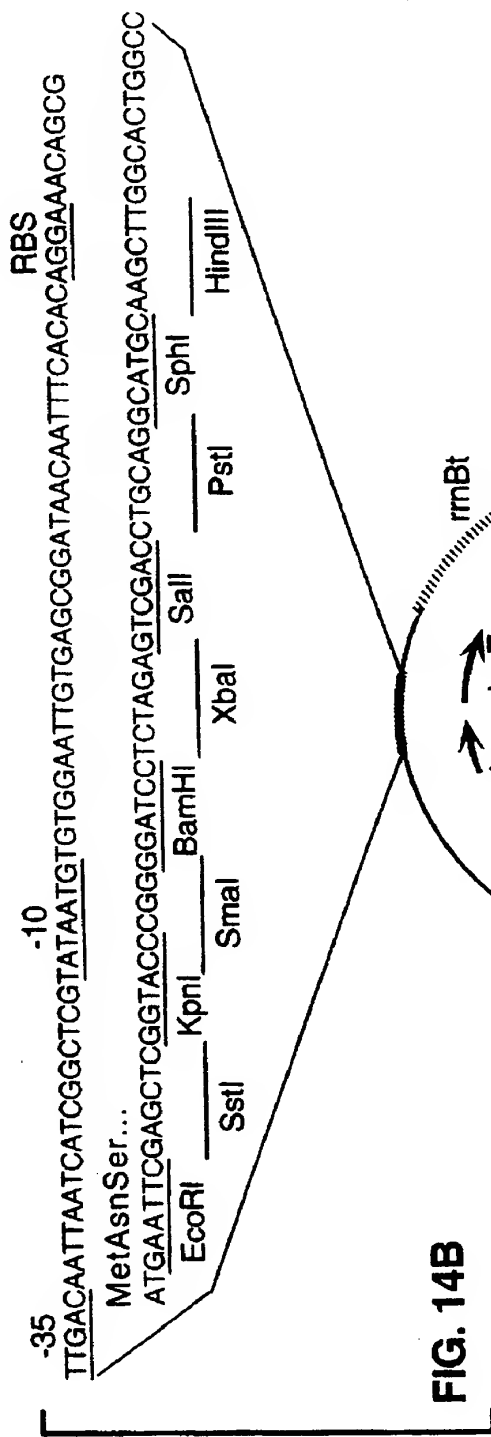


FIG. 14B

FIG. 14A

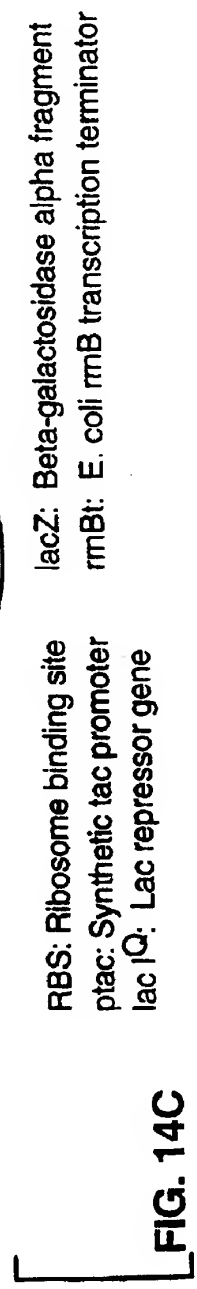
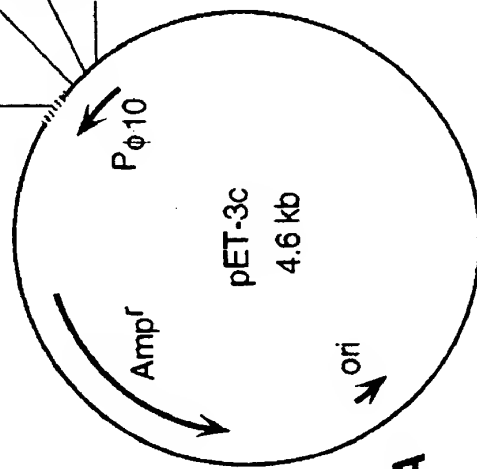
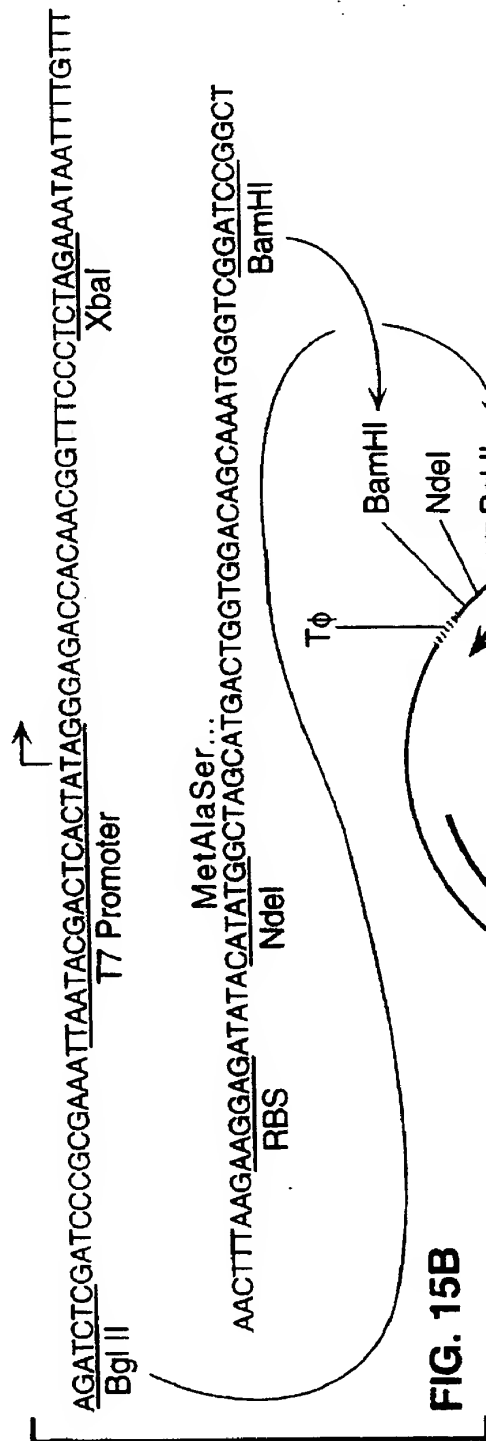


FIG. 14C



RBS: Ribosome binding site

P_{φ10}: Bacteriophage T7 φ10 promoter

Tφ: T7 φ Terminator

FIG. 15C

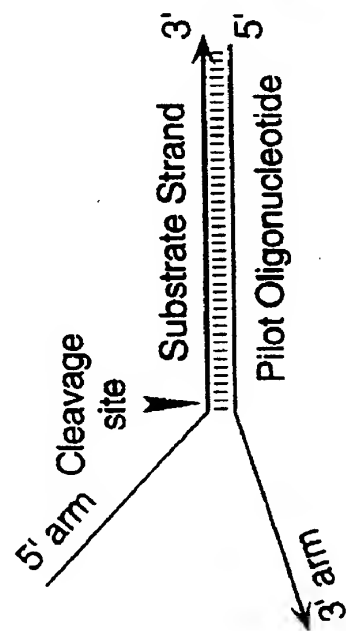


FIG. 16A

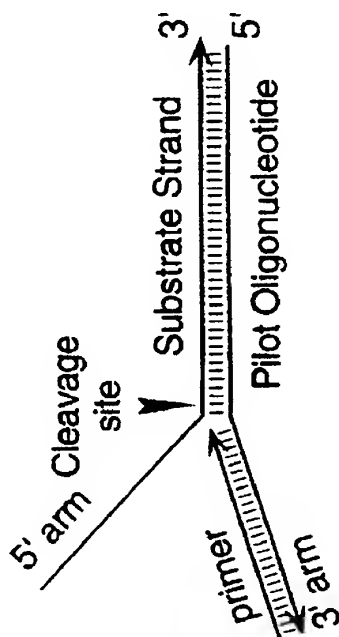


FIG. 16B

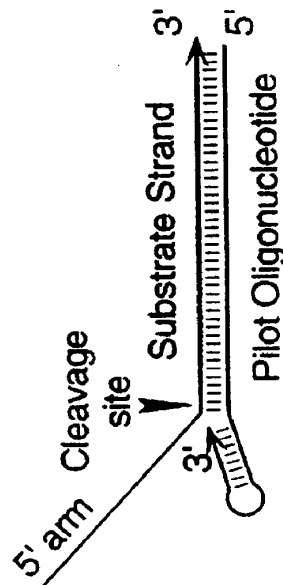


FIG. 16C

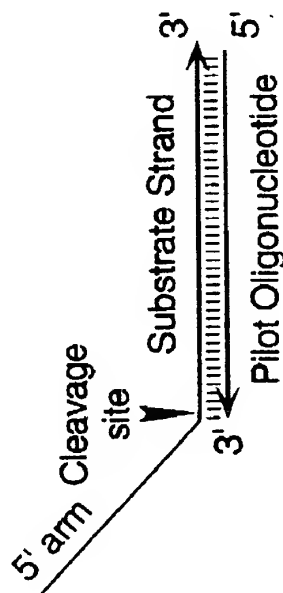


FIG. 16D

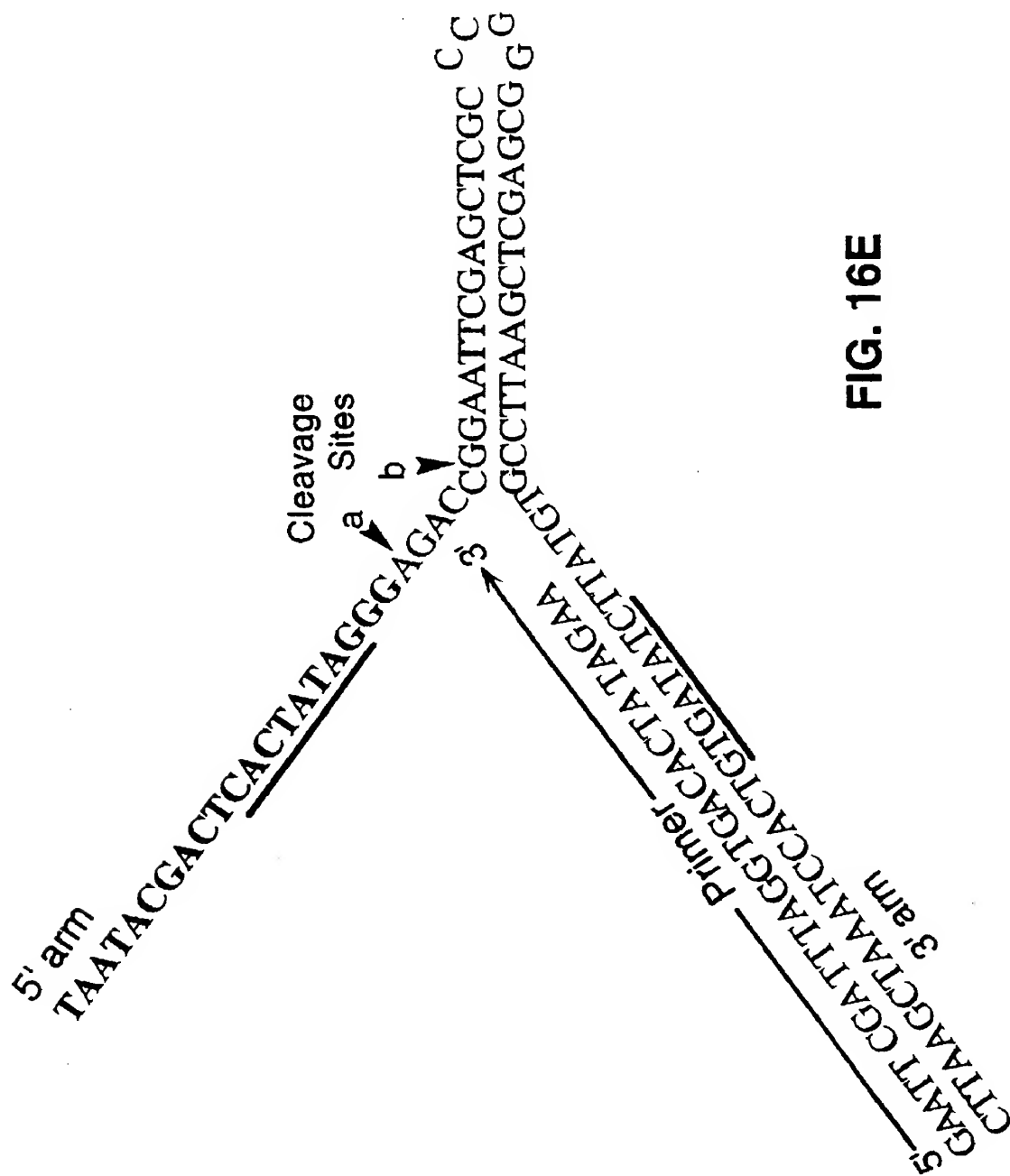


FIG. 16E

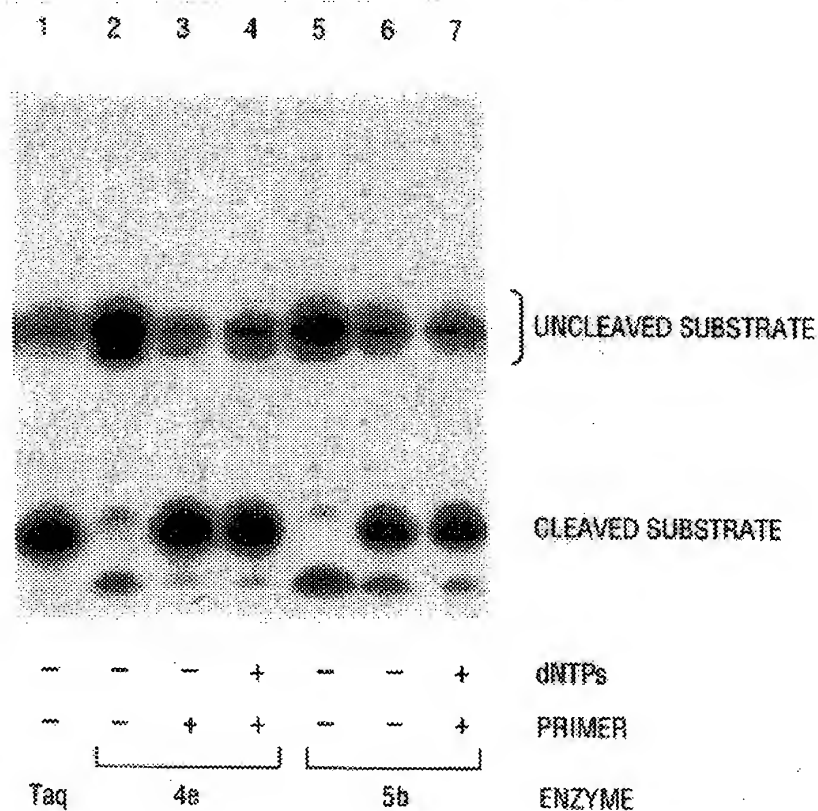


FIG. 17

UNINCORPORATED
 ^{32}P dCTP →

INCORPORATED
 ^{32}P dCMP →

ENZYME	Taq	—	Taq	4b	4c	4d	4e	4f
PRIMED M13	—	+	+	+	+	+	+	+

FIG. 18

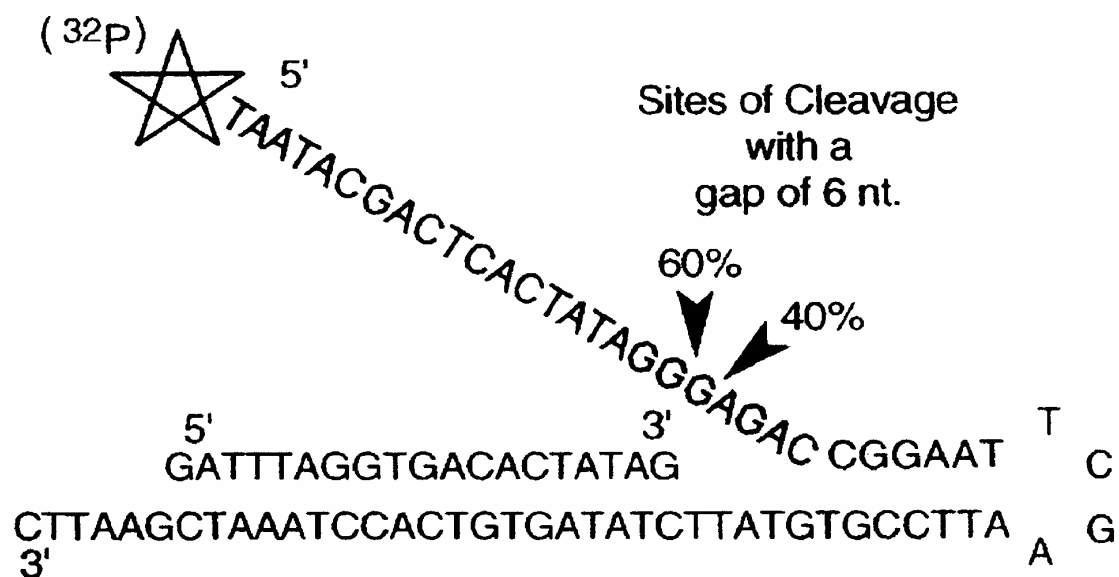


FIG. 19A

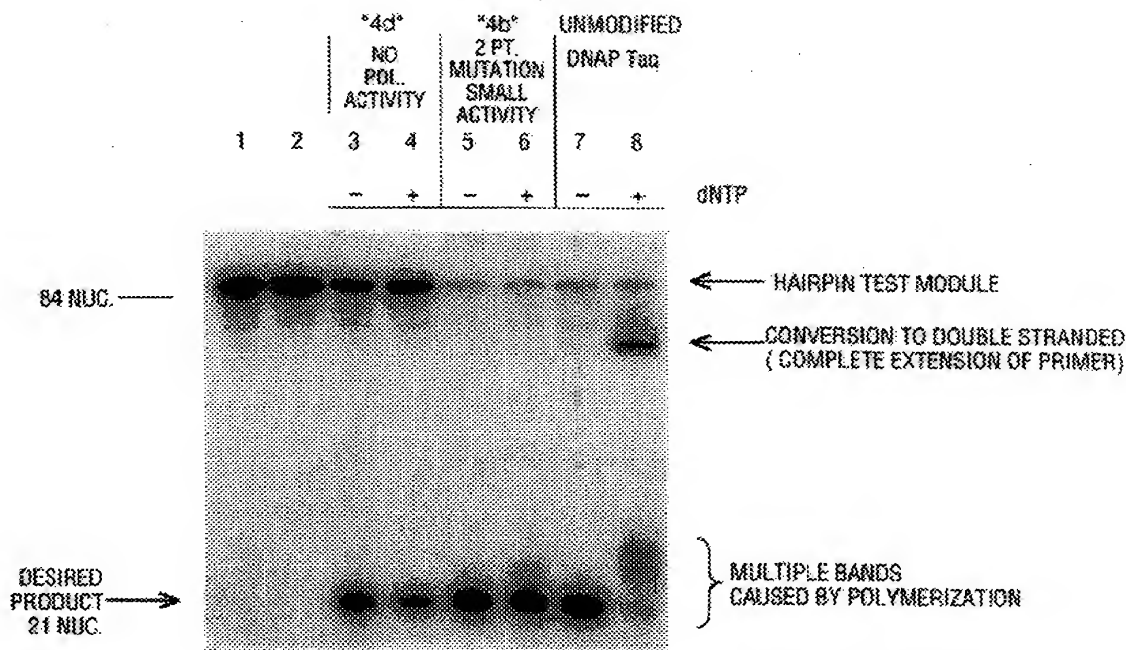
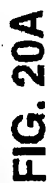


FIG. 19B



Sequence of alpha primer:



FIG. 20B

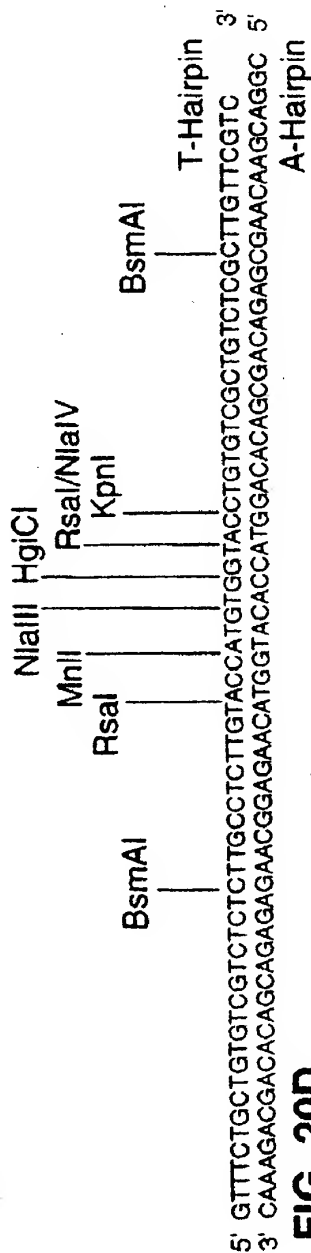
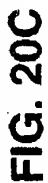


FIG. 20D

Ban II
 Sst I
 Asp 718
 Ava I
 Kpn I
 Xma I
 Sma I
 Bam HI XI
 EcoR I
 CCGCAGGGTTTCCCGAGTCACGACGTTGTAAACGACGGCCAGTGAA TTGTAATACGACTCACTATAGGGCGAA TTCGAGCTCGGTACCCCGGGGATCCCTC
 GCGGTCCTCCCAAGGGTCAGTCCTGCAACATTTTGTGCTGCCGGTCACTTAACATTATGCTGAGTGATATCCCGCTTAAGCTCGAGCCATGGGCCCTTAGGAG
 ——— -47 Forward ———
 ——— 17 ———
 ——— Pilot 30-0 ———

Sal I
 Pst I
 BspM I
 Acc I
 Sph I
 Hinc II
 Hind III
 TAGAGTCGACCTGCAGGCA TGC AAGCTTGAGTATTCATAGTGTACCTAAATAGCTTGGCGTAATCATGGTCA TAGCTGTTCCCTGTGTGAAATTGTTA
 ATCTCAGCTGGACGTCCTACGTTCCGAACTCATAGATATCACAGTGGATTTATCGAACCGCATTAGTACCAGTATCGACAAAGGACACACACTTTAACAAAT
 ——— Pilot 30-0 ———
 ——— SP6 ———
 ——— 2 ———
 ——— -48 Reverse ———

TCCGCTCACAATCCACACAACATACGA 228
 AGCGAGTGTAAAGGTGTGTGATGCT
 ——— -48 Reverse ———
 ——— 206 ———

FIG. 21



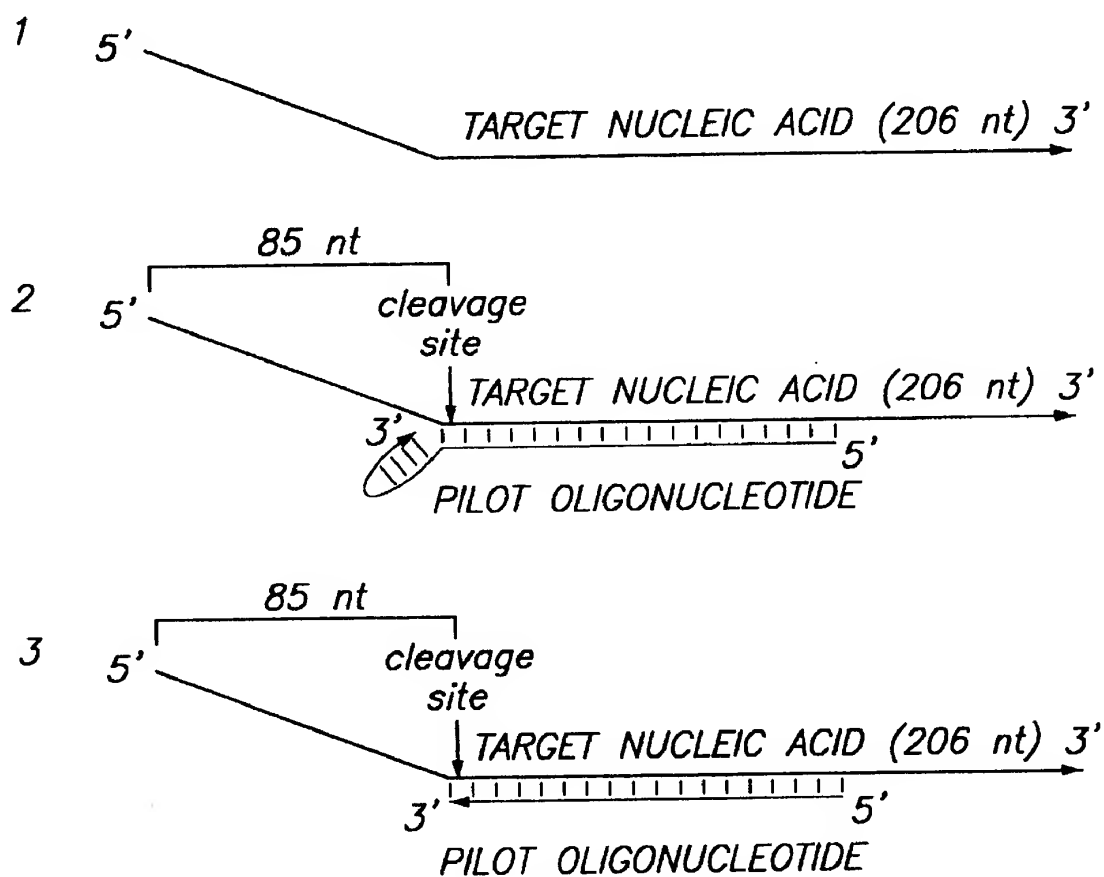


FIG. 22A

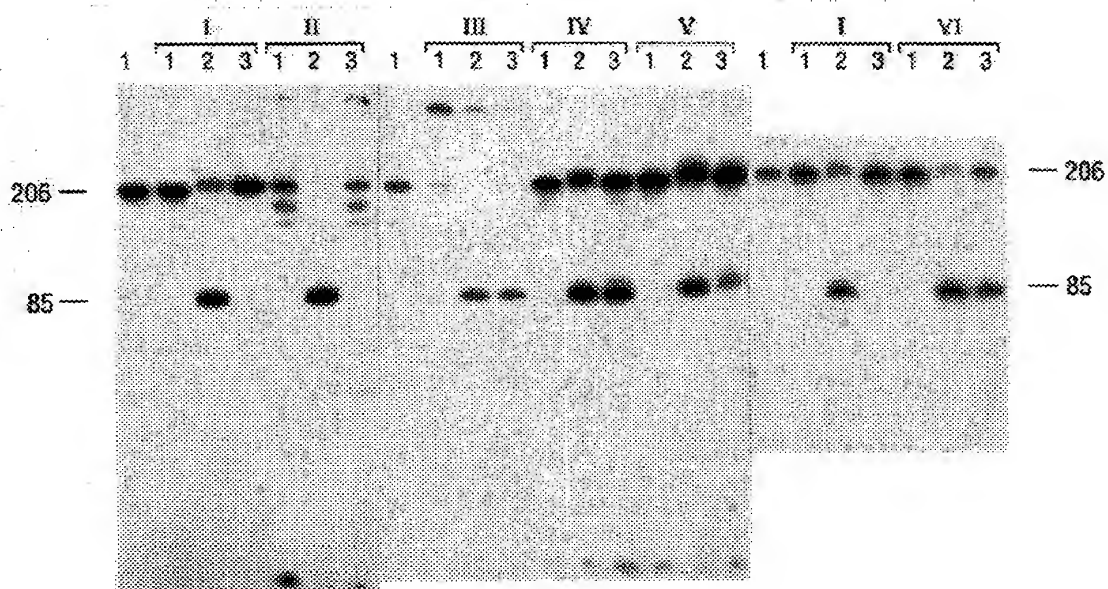


FIG. 22B

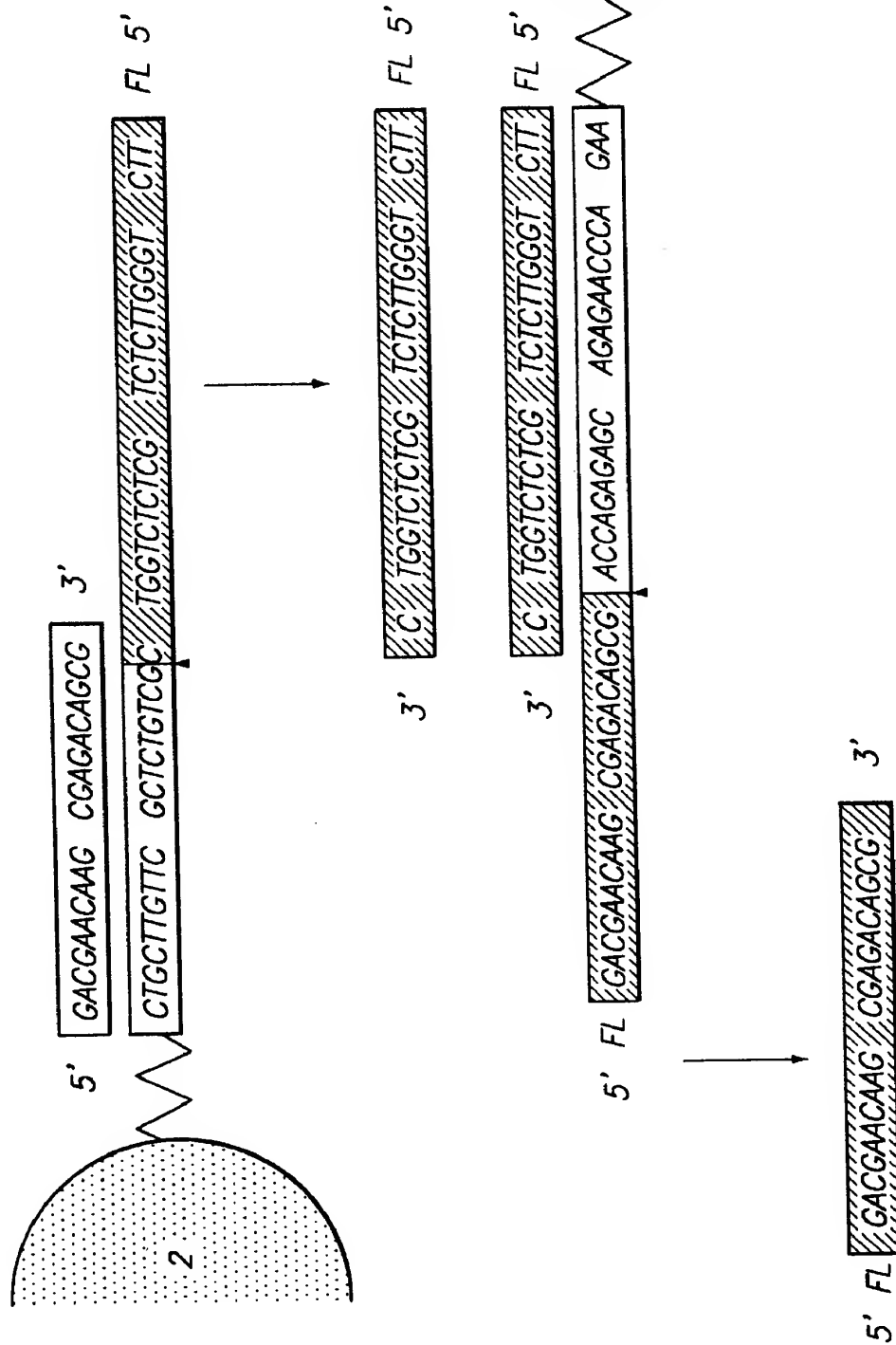


FIG. 23



CDR BEAD		T	T	T	A/T	A/T	A	A	A		
PILOT		-	-	+	-	+	+	-	-		
CLEAVASE	M	M	-	+	+	+	+	+	+	-	M

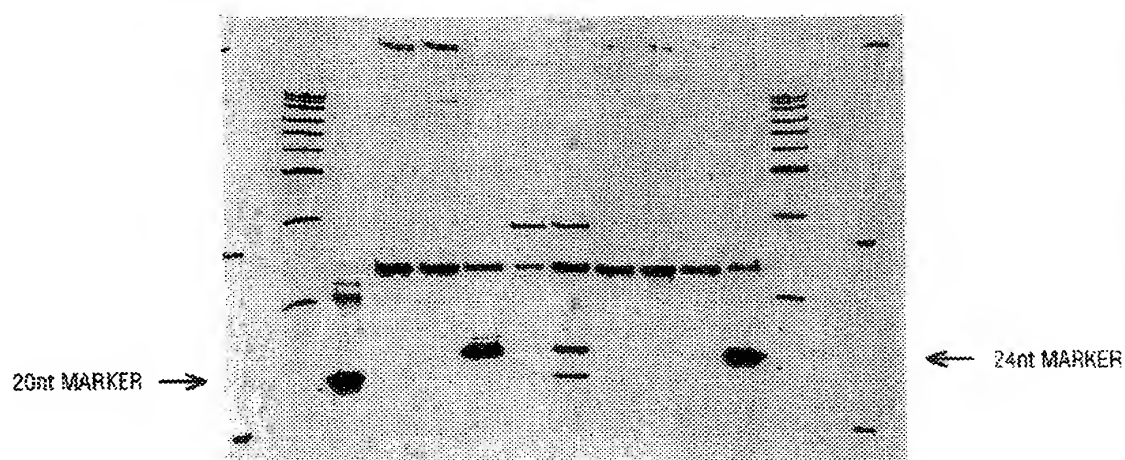


FIG. 24

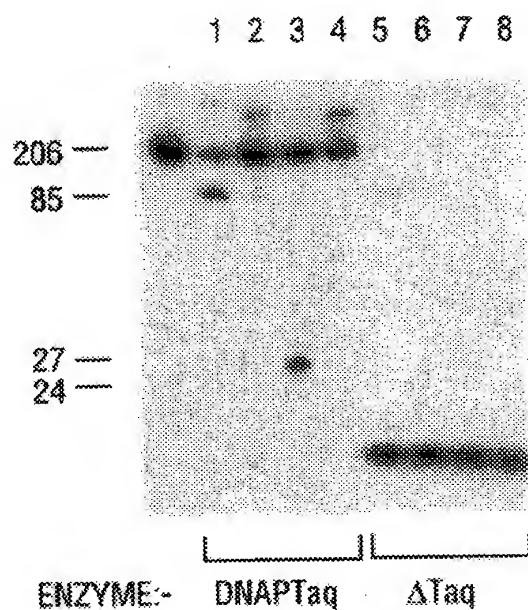


FIG. 25A

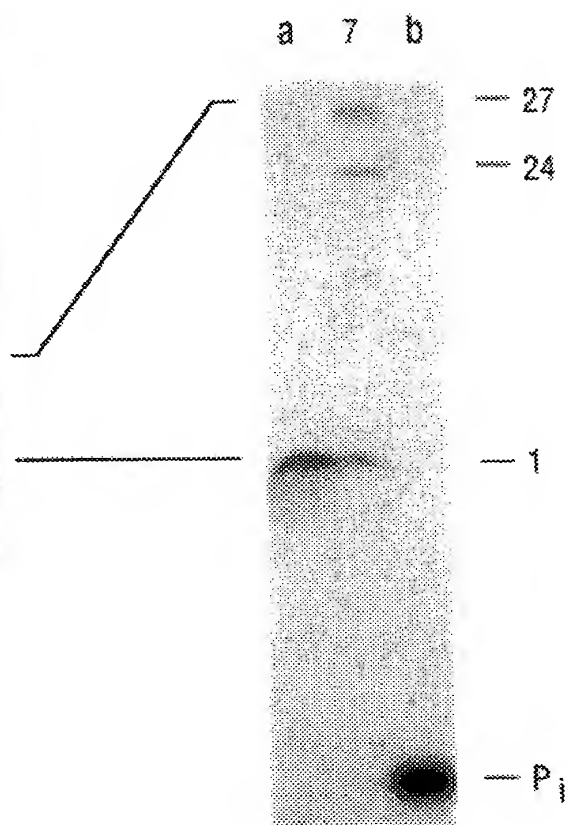


FIG. 25B



FIG. 26A

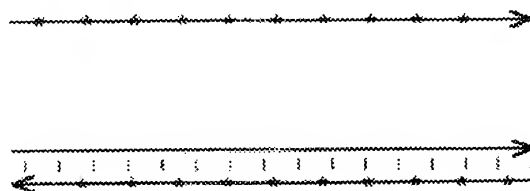
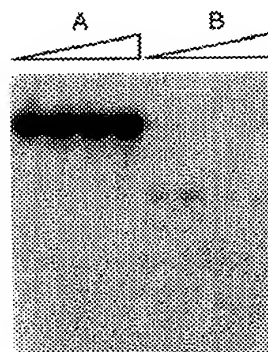


FIG. 26B

* 32p



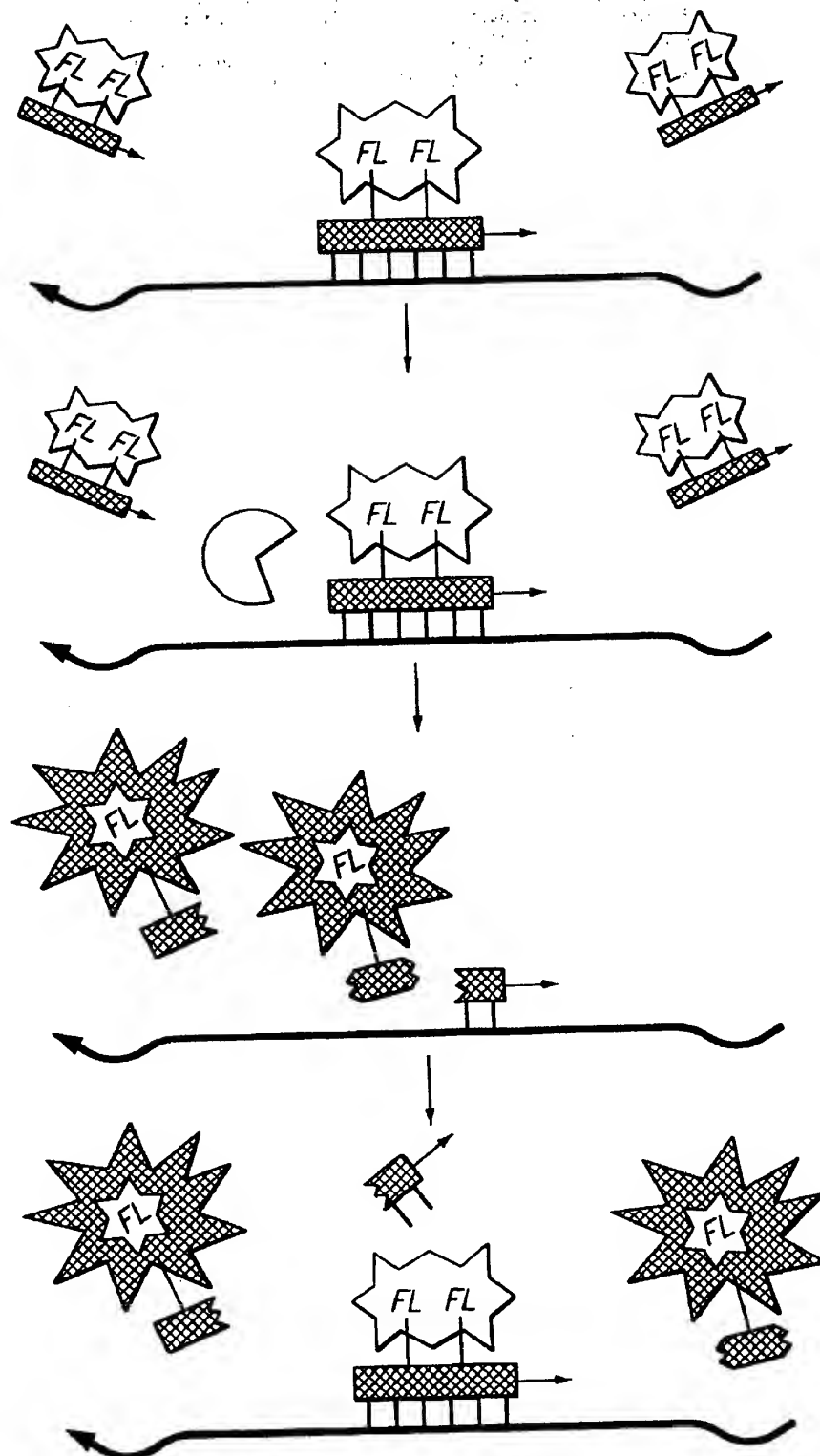


FIG. 27

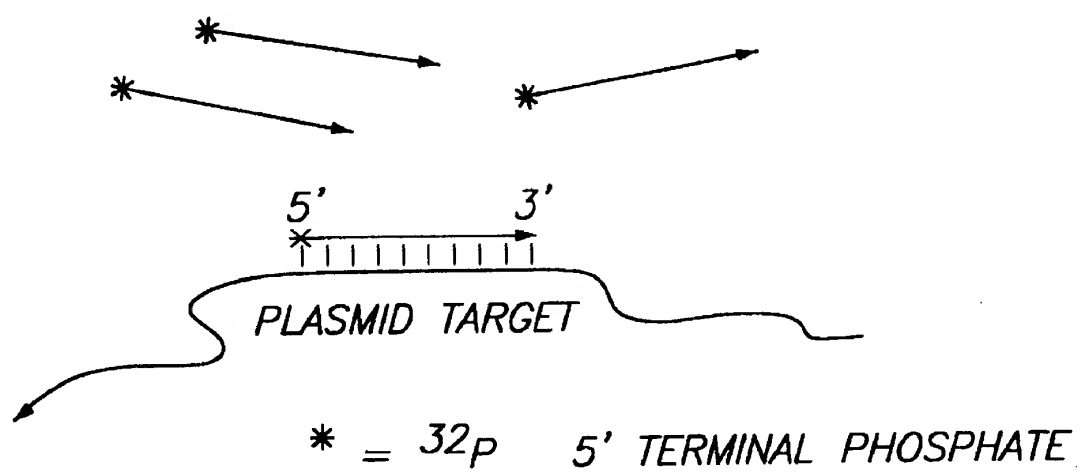


FIG. 28A

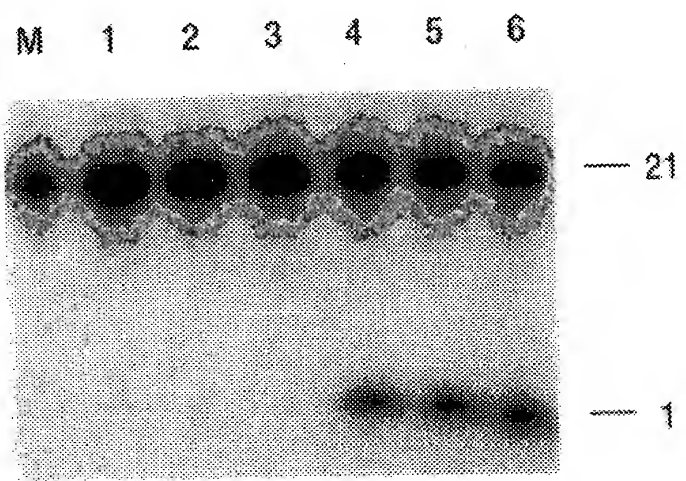


FIG. 28B



Wild-Type Substrate

Mutant Substrate



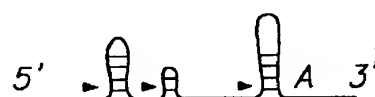
1
Denature



2
Renature



3
Add cleavage agent



▴ = cleavage site

4
Resolve reaction products

5
Detect unique cleavage "fingerprint"

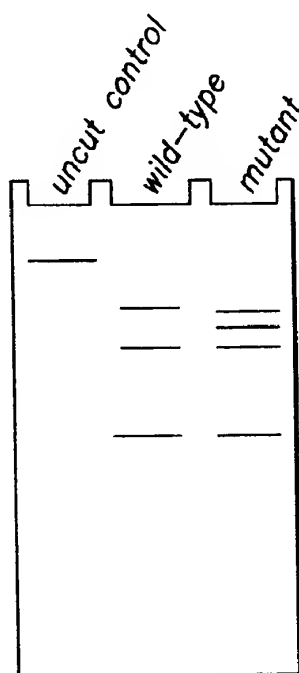


FIG. 29

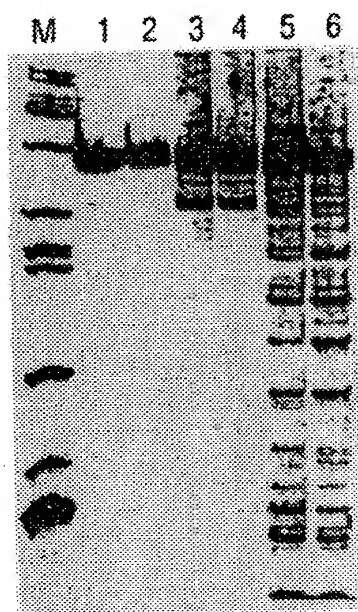
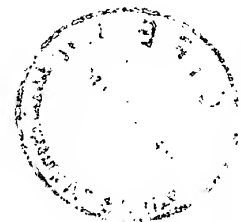


FIG. 30

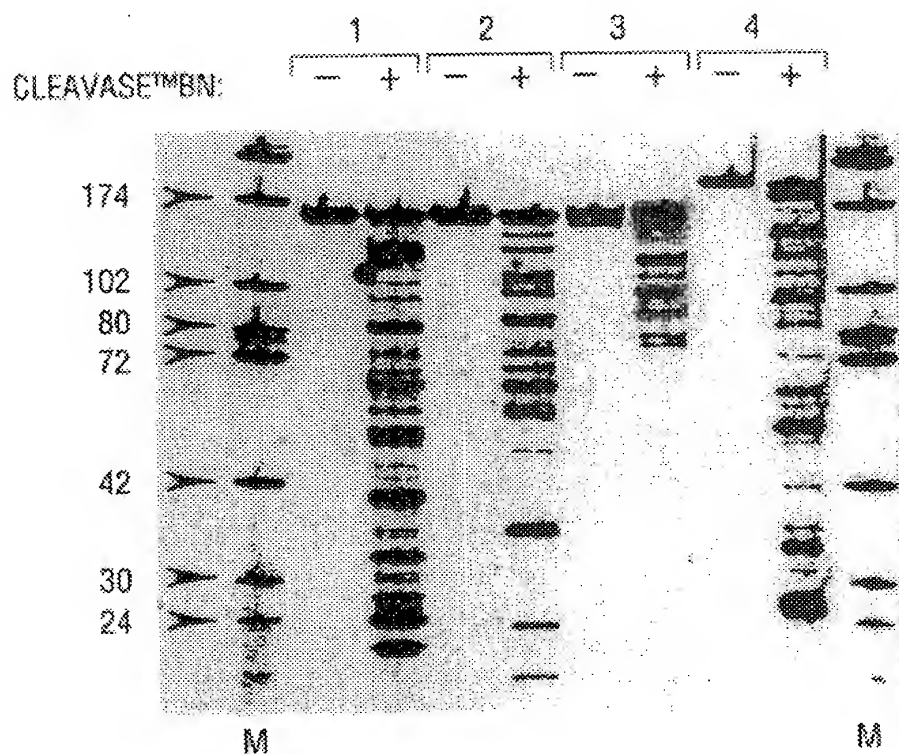


FIG. 31

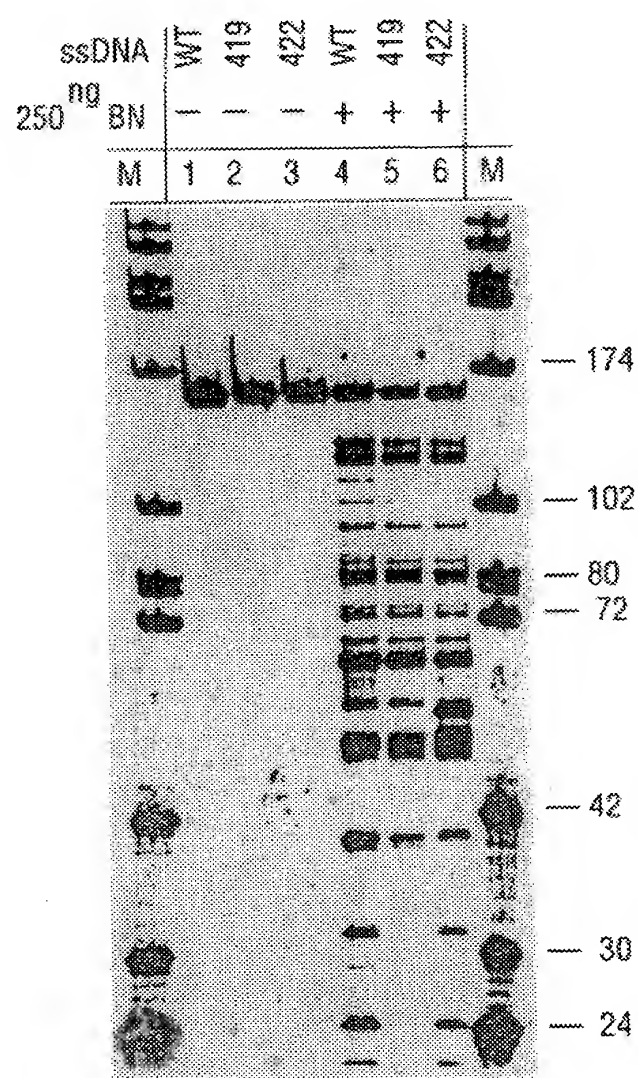


FIG. 32

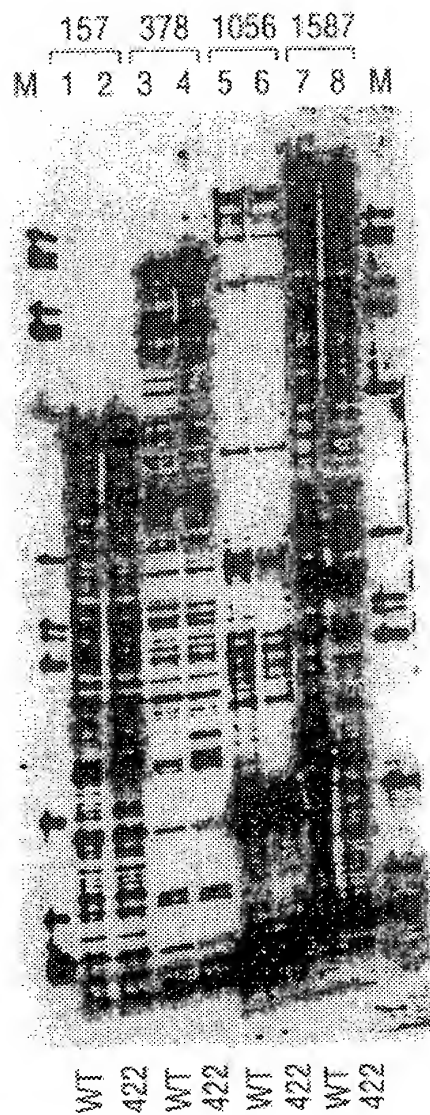


FIG. 33

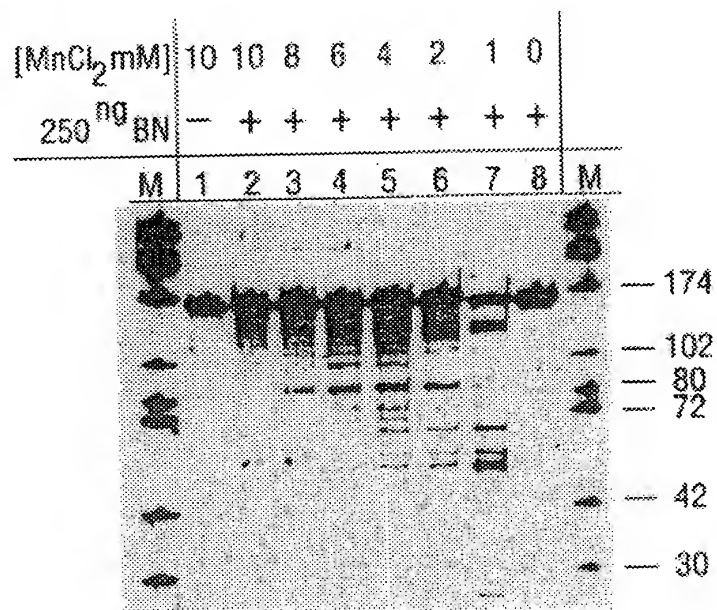


FIG. 34

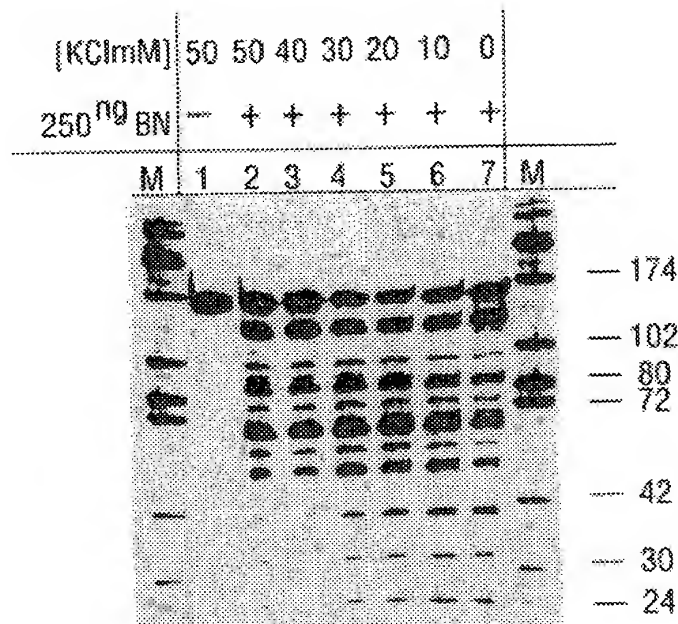


FIG. 35

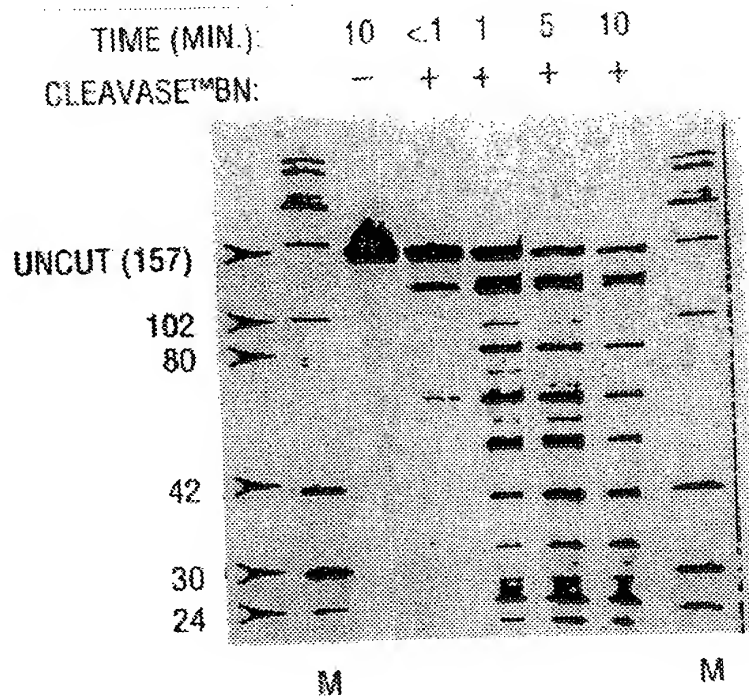


FIG. 36



TEMPERATURE (°C):	55	80	55	60	65	70	75	80
CLEAVASE™BN:	-	-	+	+	+	+	-	+

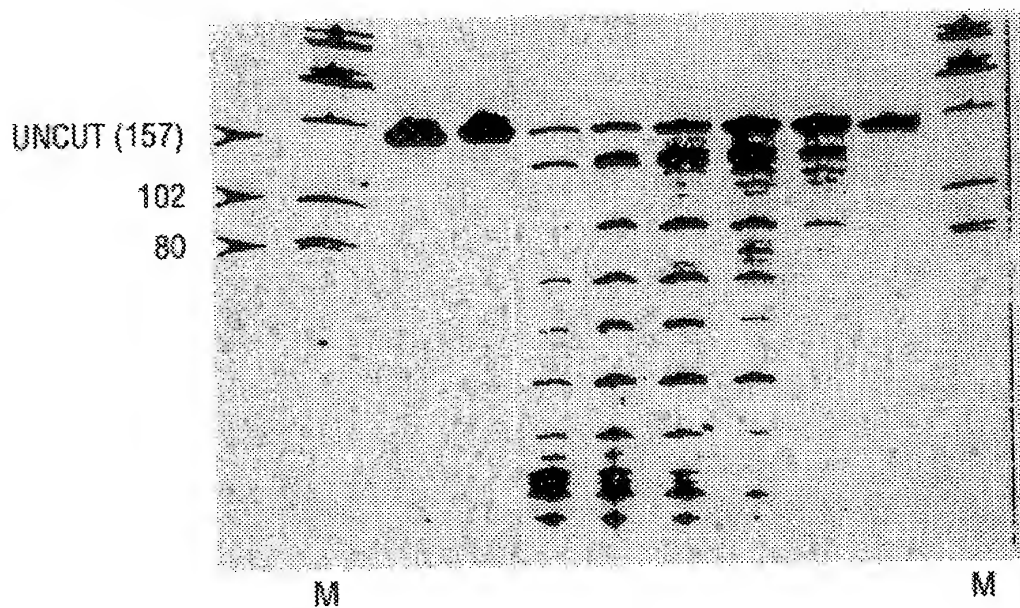


FIG. 37



CLEAVASE™BN (ng): — 10 50 100 250

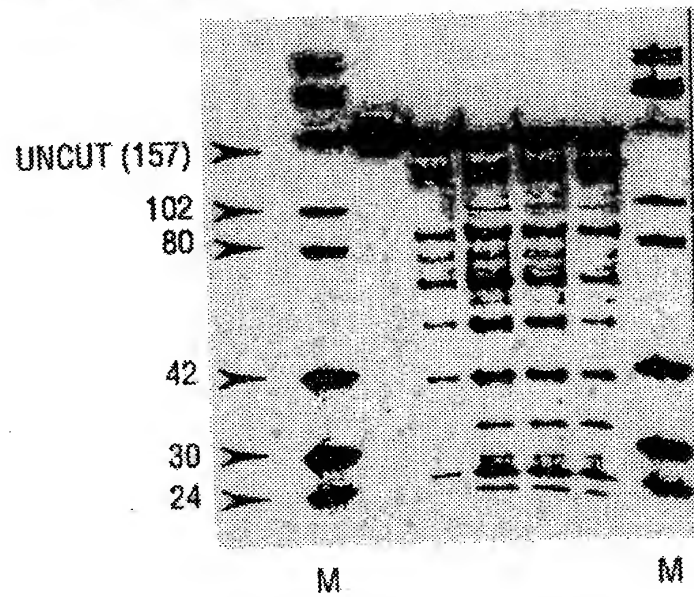


FIG. 38

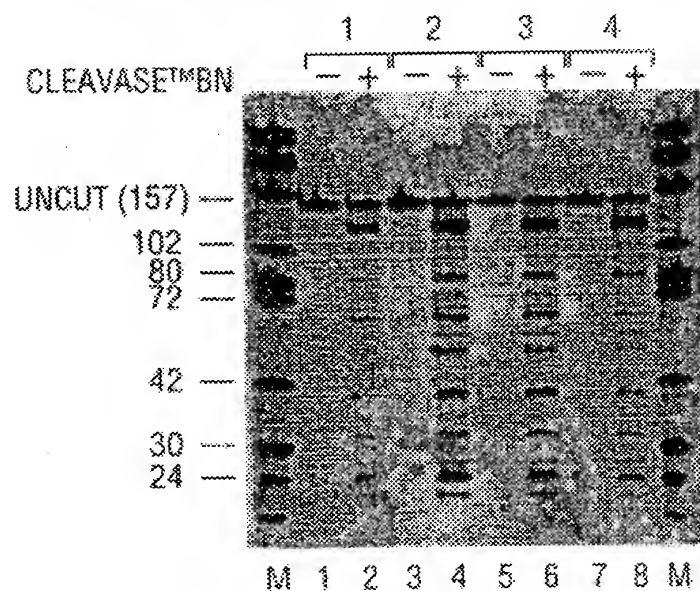


FIG. 39

STRAND	5' - BIOTIN SENSE STRAND						5' - FLUORESCCEIN ANTI-SENSE STRAND					
	WT	419	422	WT	419	422	WT	419	422	WT	419	422
ssDNA	WT	419	422	WT	419	422	WT	419	422	WT	419	422
250 ^{ng} BN	-	-	-	+	+	+	+	+	+	-	-	-
M	1	2	3	4	5	6	7	8	9	10	11	12

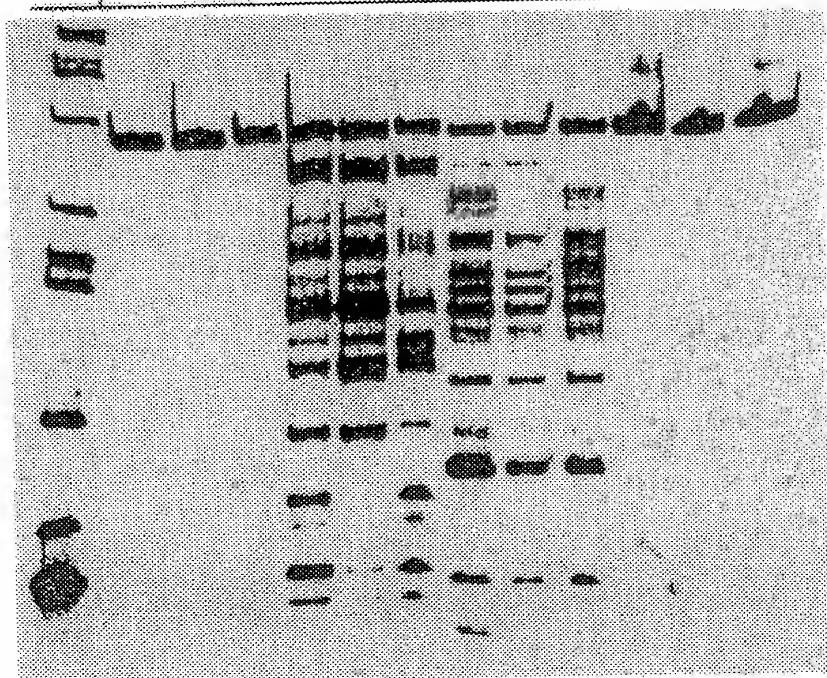


FIG. 40

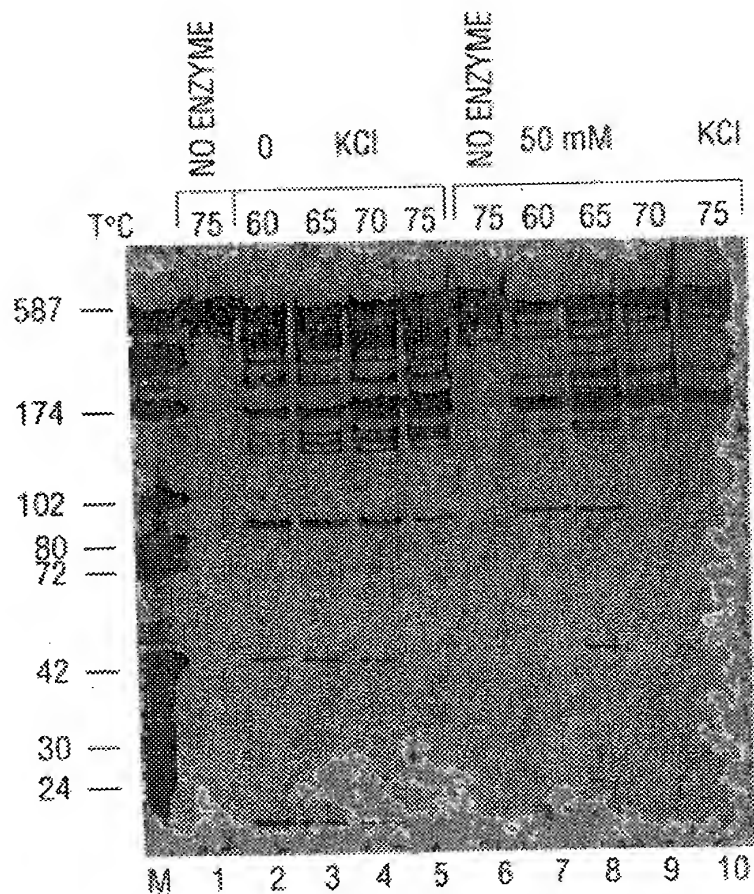


FIG. 41

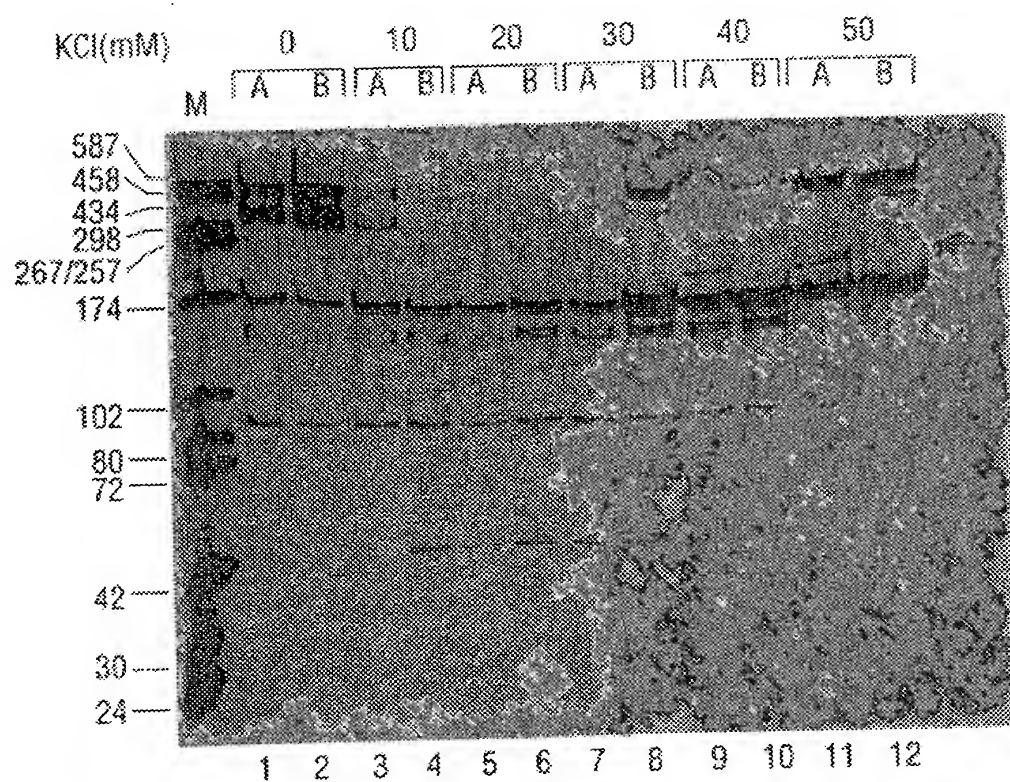


FIG. 42



CLEAVASE™BN

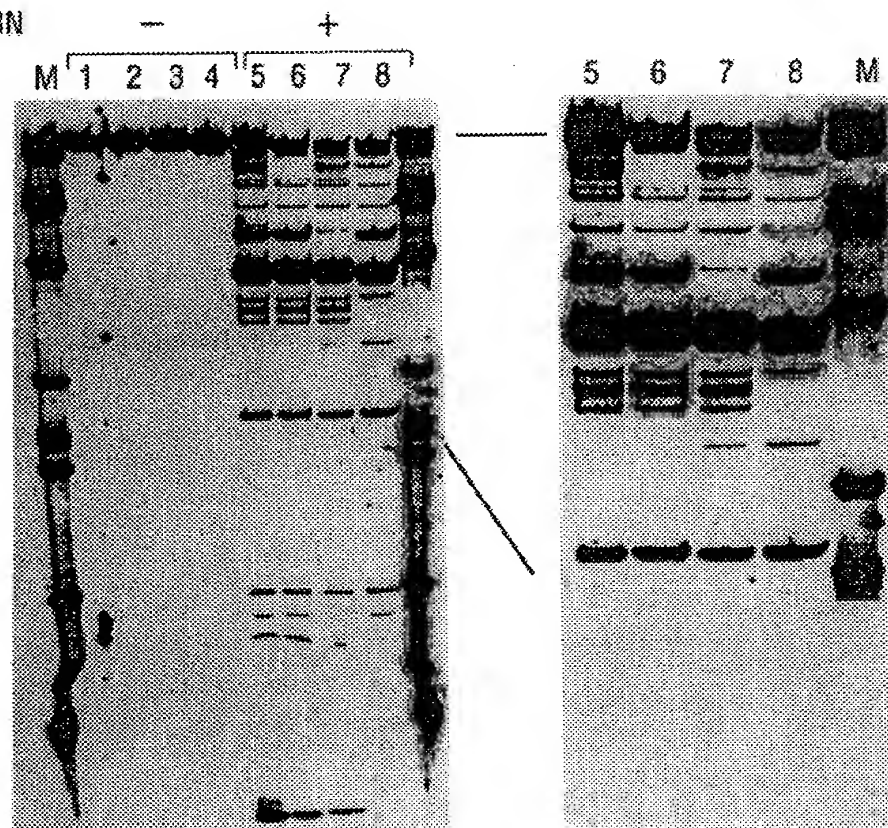


FIG. 43

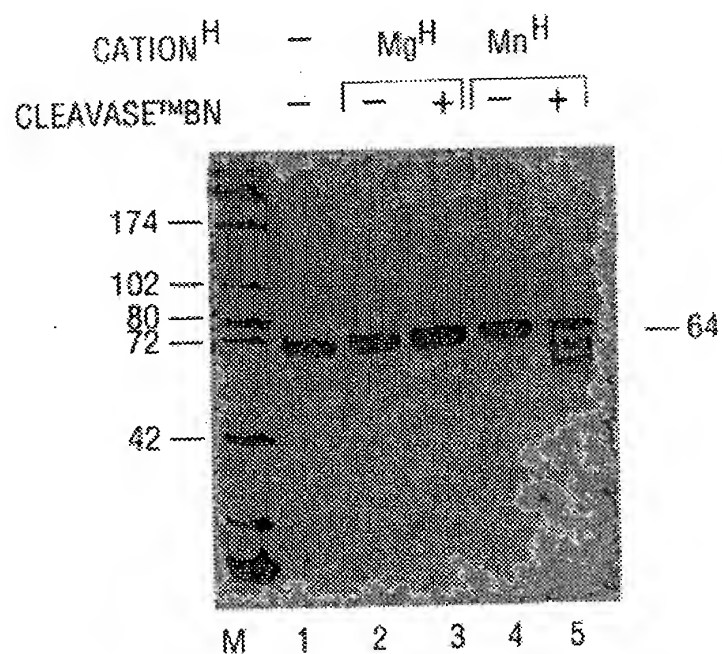
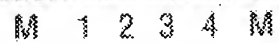


FIG. 44



60

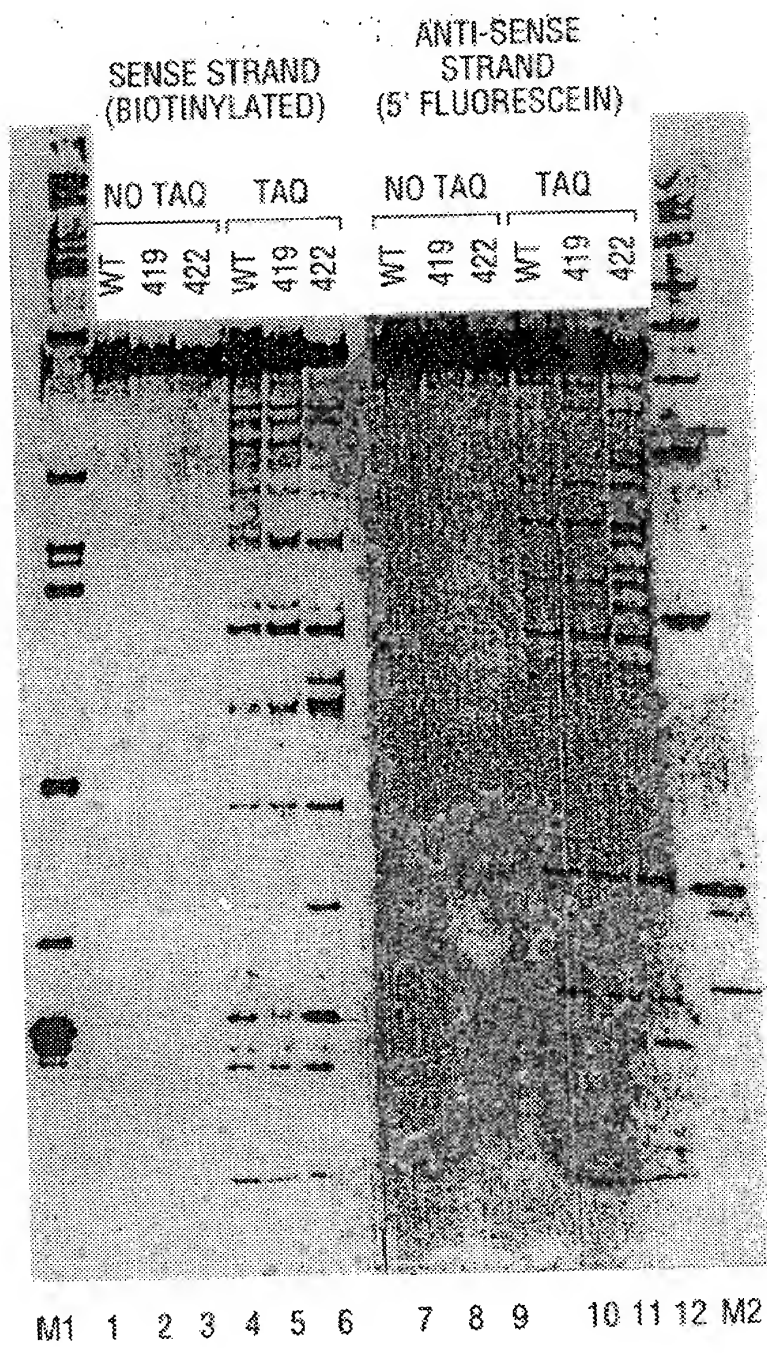


FIG. 46



U.S. GOVERNMENT PRINTING OFFICE
1964 O - 348-100
500,000
100,000
20,000
5,000
1,000
200
50
10
2
1

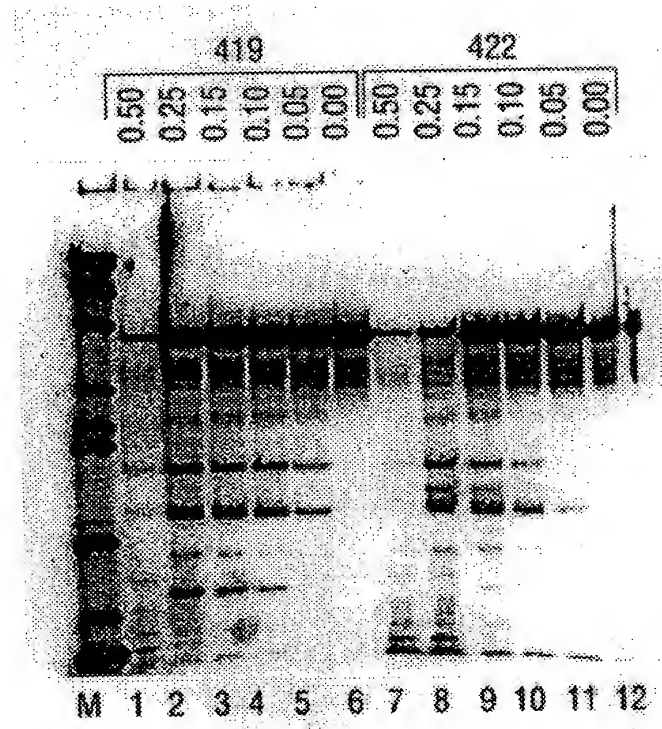


FIG. 47

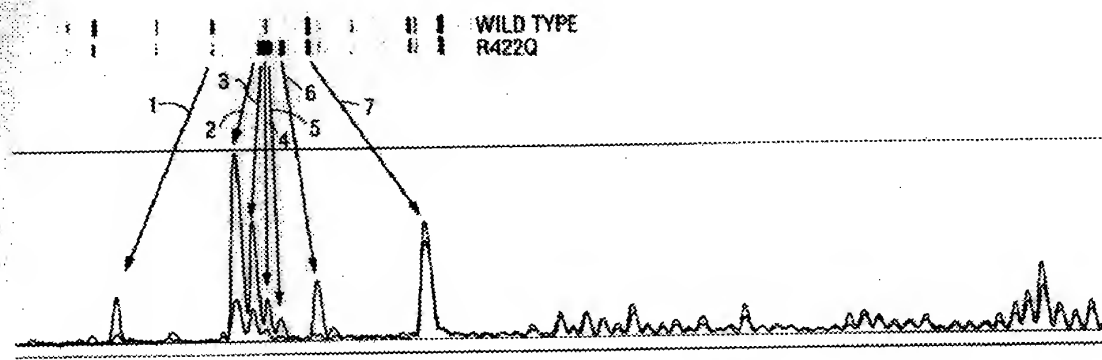


FIG. 48

L.100.8-1
(SEQ ID NO: 76) 5'GGCTGACAAGGAAGAACTCGCTGAGACAGCAGGGGACTTTCCACAAGGGG
3'CCGACTGTTCTTCTTCTTGAGCGACTCTGTCGTCCCTGAAAGGTGTTCCCC

L.46.16-10
(SEQ ID NO: 77) 5'GGCTGACAAGGAAGGAAGAACTCGCTGAGATAGCAGGGGACTTTCCACAAGGGG
3'CCGACTGTTCTTCTTCTTGAGCGACTCTATCGTCCCTGAAAGGTGTTCCCC

L.46.16-12
(SEQ ID NO: 78) 5'GGCTGACAAGGAAGGAAGAACTCGCTGAGATAGCAGGGGACTTTCCACAAGGGG
3'CCGACTGTTCTTCTTCTTGAGCGACTCTATCGTCCCTGAAAGGTGTTCCCC

L19.16-3
(SEQ ID NO: 79) 5'GGCTGACAAGGAAGGAAGAACTCGCTGAGACAGCAGGGGACTTTCCACAAGGGG
3'CCGACTGTTCTTCTTCTTGAGCGACTCTGTCGTCCCTGAAAGGTGTTCCCC

L.CEM/251
(SEQ ID NO: 80) 5'GGCTGACAAGGAAGGAAGAACTCGCTGAAACAGCAGGGGACTTTCCACAAGGGG
3'CCGACTGTTCTTCTTCTTGAGCGACTTTGTCGTCCCTGAAAGGTGTTCCCC

L.36.8-3
(SEQ ID NO: 81) 5'GGCTGACAAGGAAGGAAGAACTCGCTGAGACAGCAGGGGACTTTCCACAAGGGG
3'CCGACTGTTCTTCTTCTTGAGCGACTCTGTCGTCCCTGAAAGGTGTTCCCC

FIG. 49A



100

L.100.8-1
(SEQ ID NO: 76)

ATGTTACGGGGAGGTACTGGGGAGGAGCCGGTCGGGAACGCCACTCTCT
TACAATGCCCCCTCCATGACCCCTCCTCGGCCAGCCCTTGCGGGTGAGAGA

L.46.16-10
(SEQ ID NO: 77)

ATGTTATGGGGAGG-----AGCCGGTCGGGAACACCCACTTTCT
TACAATACCCCTCC-----TCGGCCAGCCCTTGTTGGGTGAAAGA

L.46.16-12
(SEQ ID NO: 78)

ATGTTATGGGGAGG-----AGCCGGTCGGGAACACCCACTTTCT
TACAATACCCCTCC-----TCGGCCAGCCCTTGTTGGGTGAAAGA

L19.16-3
(SEQ ID NO: 19)

ATGTTACGGGGAGGTACTGGGGAGGAGCCGGTCGGGAACGCCCTCTCT
TACAATGCCCCCTCCATGACCCCTCCTCGGCCAGCCCTTGCGGGGAGAGA

L.CEM/251
(SEQ ID NO: 80)

ATGTTACGGGGAGGTACTGGGAAGGAGCCGGTCGGGAACGCCACTTTCT
TACAATGCCCCCTCCATGACCCCTCCTCGGCCAGCCCTTGCGGGGTGAAAGA

L.36.8-3
(SEQ ID NO: 81)

ATGTTACGGAGAGGTACTGGGGAGGAGCCGGTCGGGAACGCCACTCTCT
TACAATGCCTCTCCATGACCCCTCCTCGGCCAGCCCTTGCGGGGTGAGAGA

FIG. 49B





L. 100.8-1

5'TGATGTATAAATAATCACTGCATTTCGCTCTGTATTCAAGTCAGTCGCTCTGCGGA
3'ACTACATATTTATAGTGACGTAAGCGAGACATAAGTCAGCGAGACGCCCT

150

L. 46.16-10

5'TGATGTATAAATAATCACTGCATTTCGCTCTGTATTCAAGTCAGTCGCTCTGCGGA
3'ACTACATATTTATAGTGACGTAAGCGAGACATAAGTCAGCGAGACGCCCT

L. 46.16-12

5'TGGTGTATAAATAATCACTGCATTTCGCTCTGTATTCAAGTCAGTCGCTCTGCGGA
3'ACCACATATTTATAGTGACGTAAGCGAGACATAAGTCAGCGAGACGCCCT

L. 19.16-3

5'TGATGTATAAATAATCACTGCATTTCGCTCTGTATTCAAGTCAGTCGCTCTGCGGA
3'ACTACATATTTATAGTGACGTAAGCGAGACATAAGTCAGCGAGACGCCCT

L. CEM/251

5'TGATGTATAAATAATCACTGCATTTCGCTCTGTATTCAAGTCAGTCGCTCTGCGGA
3'ACTACATATTTATAGTGACGTAAGCGAGACATAAGTCAGCGAGACGCCCT

L. 36.8-3

5'TGATGTATAAATAATCACTGCATTTCGCTCTGTATTCAAGTCAGTCGCTCTGCGGA
3'ACTACATATTTATAGTGACGTAAGCGAGACATAAGTCAGCGAGACGCCCT

FIG. 49C



L. 100.8-1

GAGGCTGGCAGATTGAGCCCTGGGAGGTTCTCTCCAGCACTAGCAGGTAG
CTCCGACCGTCTAACTCGGGACCCCTCCAAGAGAGGTCGTGATCGTCCATC

200

L. 46.16-10

GAGGCTGGCAGATTGAGCCCTGGGAGGTTCTCTCCAGCACTAGCAGGTAG
CTCCGACCGTCTAACTCGGGACCCCTCCAAGAGAGGTCGTGATCGTCCATC

L. 46.16-12

GAGGCTGGCAGATTGAGCCCTGGGAGGTTCTCTCCAGCACTAGCAGGTAG
CTCCGACCGTCTAACTCGGGACCCCTCCAAGAGAGGTCGTGATCGTCCATC

L. 19.16-3

GAGGCTGGCAGATTGAGCCCTGGGAGGTTCTCTCCAGCACTAGCAGGTAG
CTCCGACCGTCTAACTCGGGACCCCTCCAAGAGAGGTCGTGATCGTCCATC

L. CEM/251

GAGGCTGGCAGATTGAGCCCTGGGAGGTTCTCTCCAGCACTAGCAGGTAG
CTCCGACCGTCTAACTCGGGACCCCTCCAAGAGAGGTCGTGATCGTCCATC

L. 36.8-3

GAGGCTGGCAGATTGAGCCCTAGGAGGTTCTCTCCAGCACTAGCAGGTAG
CTCCGACCGTCTAACTCGGGATCCTCCAAGAGAGGTCGTGATCGTCCATC

FIG. 49D

250

L. 100. 8 -1 5'AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTGGCCGGTGCTGGG
(SEQ ID NO: 76) 3'TCGGACCCACAAGGGACCATCTGAGAGTGGTCGTGAACCGGCCACGACCC

L. 46.16-10 5'AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTAGCCAGTGCTGGG
(SEQ ID NO: 77) 3'TCGGACCCACAAGGGACGATCTGAGAGTGGTCGTGAATCGGTCACGACCC

L. 46.16-12 5'AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTGGCCAGTGCTGGG
(SEQ ID NO: 78) 3'TCGGACCCACAAGGGACGATCTGAGAGTGGTCGTGAACCGGTCACGACCC

L. 19.16-3 5'AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTGGCCGGTGCTGGG
(SEQ ID NO: 79) 3'TCGGACCCACAAGGGACGATCTGAGAGTGGTCGTGAACCGGCCACGACCC

L. CEM/251 5'AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTGGCCGGTGCTGGG
(SEQ ID NO: 80) 3'TCGGACCCACAAGGGACGATCTGAGAGTGGTCGTGAACCGGCCACGACCC

L. 36.8-3 5'AGCCTGAGTGTTCCCTGCTAAACTCTCACCAGCACTTGGCCGGTGCTGGG
(SEQ ID NO: 81) 3'TCGGACTCACAAAGGGACGATTTGAGAGTGGTCGTGAACCGGCCACGACCC

HAIRPIN

FIG. 49E



300

L. 100. 8 -1 (SEQ ID NO: 76)	CAGAGTGGCTCCACGCTTGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC GTCTCAACGAGGTGCGAACGAACGAAATTTCTGGAGAGTTATTTTCGACGC
L. 46.16-10 (SEQ ID NO: 77)	CAGAGTGGCTCCACGCTTGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC GTCTCAACGAGGTGCGAACGAACGAAATTTCTGGAGAGTTATTTTCGACGG
L. 46.16-12 (SEQ ID NO: 78)	CAGAGTGGCTCCACGCTTGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC GTCTCAACGAGGTGCGAACGAACGAAATTTCTGGAGAGTTATTTTCGACGG
L. 19.16-3 (SEQ ID NO: 79)	CAGAGTGGCTCCACGCTTGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC GTCTCAACGAGGTGCGAACGAACGAAATTTCTGGAGAGTTATTTTCGACGG
L. CEM/251 (SEQ ID NO: 80)	CAGAGTGACTCCACGCTTGCTTGCTTAAAGCCCTCTTCAATAAAGCTGCC GTCTCACTGAGGTGCGAACGAACGAAATTTCTGGAGAGTTATTTTCGACGG
L. 36.8-3 (SEQ ID NO: 81)	CAGAGCGGCTCCACGCTTGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC GTCTCGCCGAGGTGCGAACGAACGAAATTTCTGGAGAGTTATTTTCGACGG

HAIRPIN

FIG. 49F



L.100.8-1	<div>350</div> <div>5'ATTTTAGAAGTAGGCCAGTGTGTGTTCCCATCTCTCCTAGCCGCCGCTG G 3'</div> <div>3'TAAAATCTTCATCCGGTCACACACAAAGGTTAGAGAGGATCGGCGGGGAC C 5'</div>
L.46.16-10	<div>5'ATTTTAGAAGTAAGCCAGTGTGTGTTCCCATCTCTCCTAGCCGCCGCTG G 3'</div> <div>3'TAAAATCTTCATTCGGTCACACACAAAGGTTAGAGAGGATCGGCGGGGAC C 5'</div>
L.46.16-12	<div>5'ATTTTAGAAGTAAGCCAGTGTGTGTTCCCATCTCTCCTAGCCGCCGCTG G 3'</div> <div>3'TAAAATCTTCATTCGGTCACACACAAAGGTTAGAGAGGATCGGCGGGGAC C 5'</div>
L.19.16-3	<div>5'ATTTTAGAAGTAGGCTAGTGTGTGTTCCCATCTCTCCTAGCCGCCGCTG G 3'</div> <div>3'TAAAATCTTCATCCGATCACACACAAAGGTTAGAGAGGATCGGCGGGGAC C 5'</div>
L.CEM/251	<div>5'ATTTTAGAAGTAGTGTGTGTTCCCATCTCTCCTAGCCGCCGCTG G 3'</div> <div>3'TAAAATCTTCATTCGATCACACACAAAGGTTAGAGAGGATCGGCGGGGAC C 5'</div>
L.36.8-3	<div>5'ATTTTAGAAGTAGGCTAGTGTGTGTTCCCATCTCTCCTAGCCGCCGCTG G 3'</div> <div>3'TAAAATCTTCATCCGATCACACACAAAGGTTAGAGAGGATCGGCGGGGAC C 5'</div>

FIG. 49G



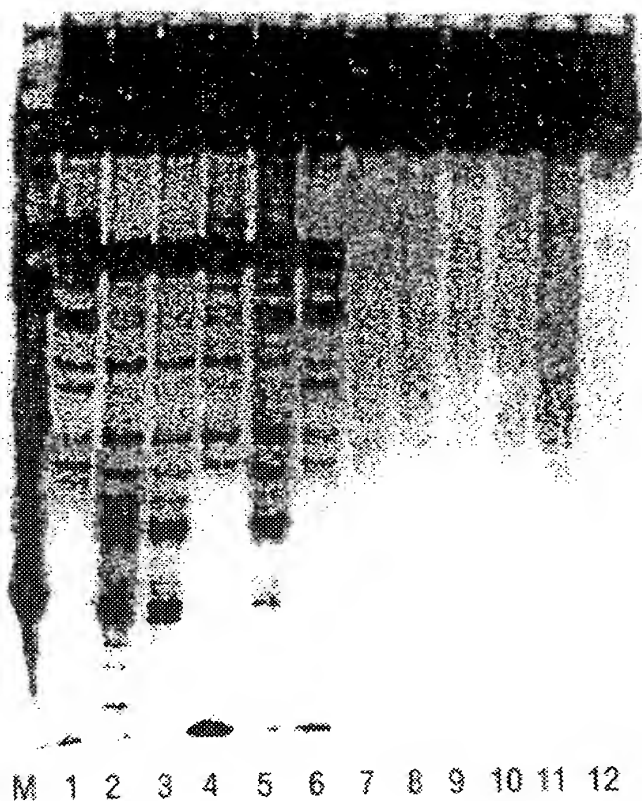


FIG. 50

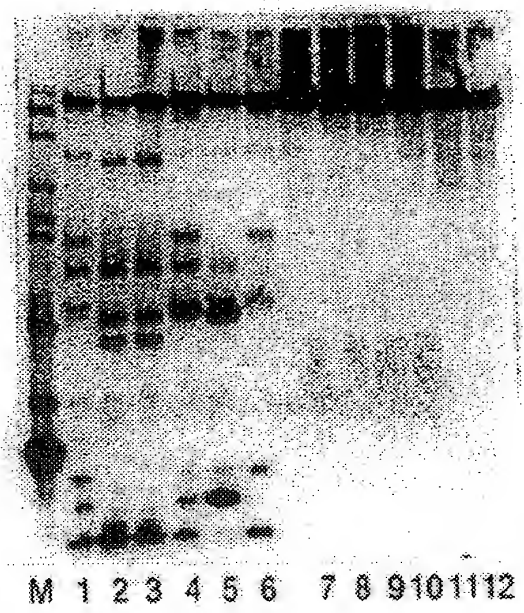


FIG. 51

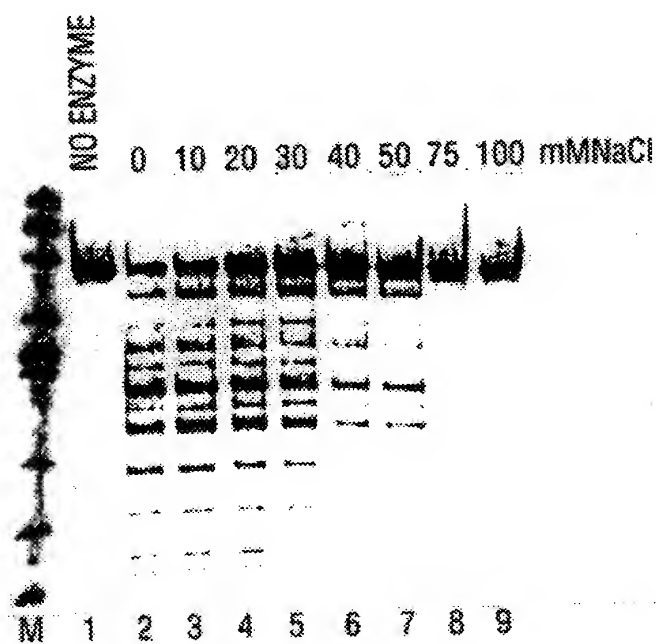


FIG. 52

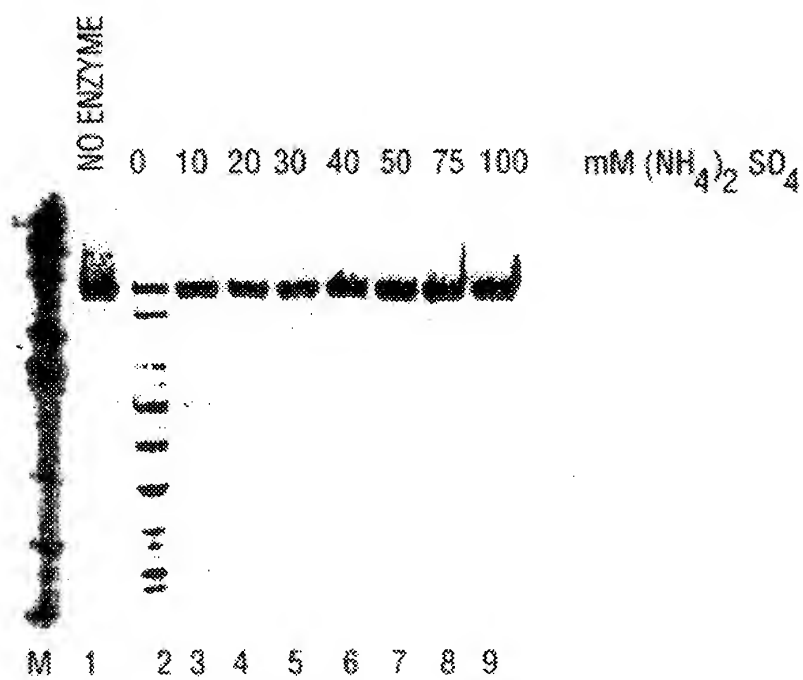


FIG. 53

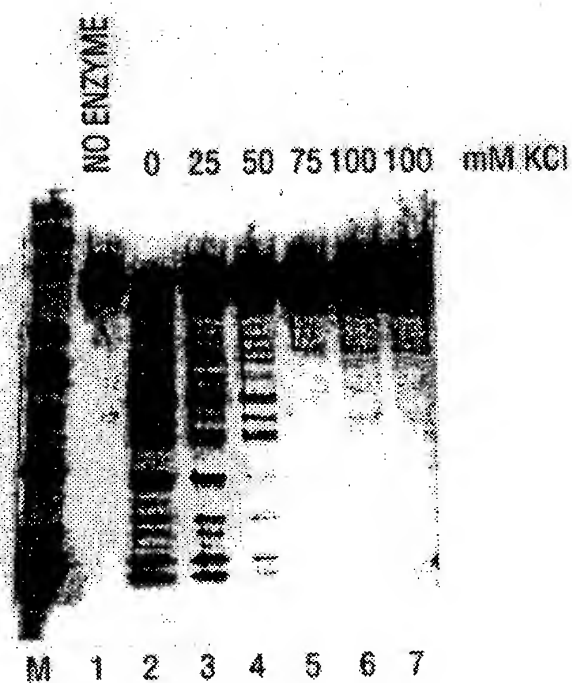


FIG. 54

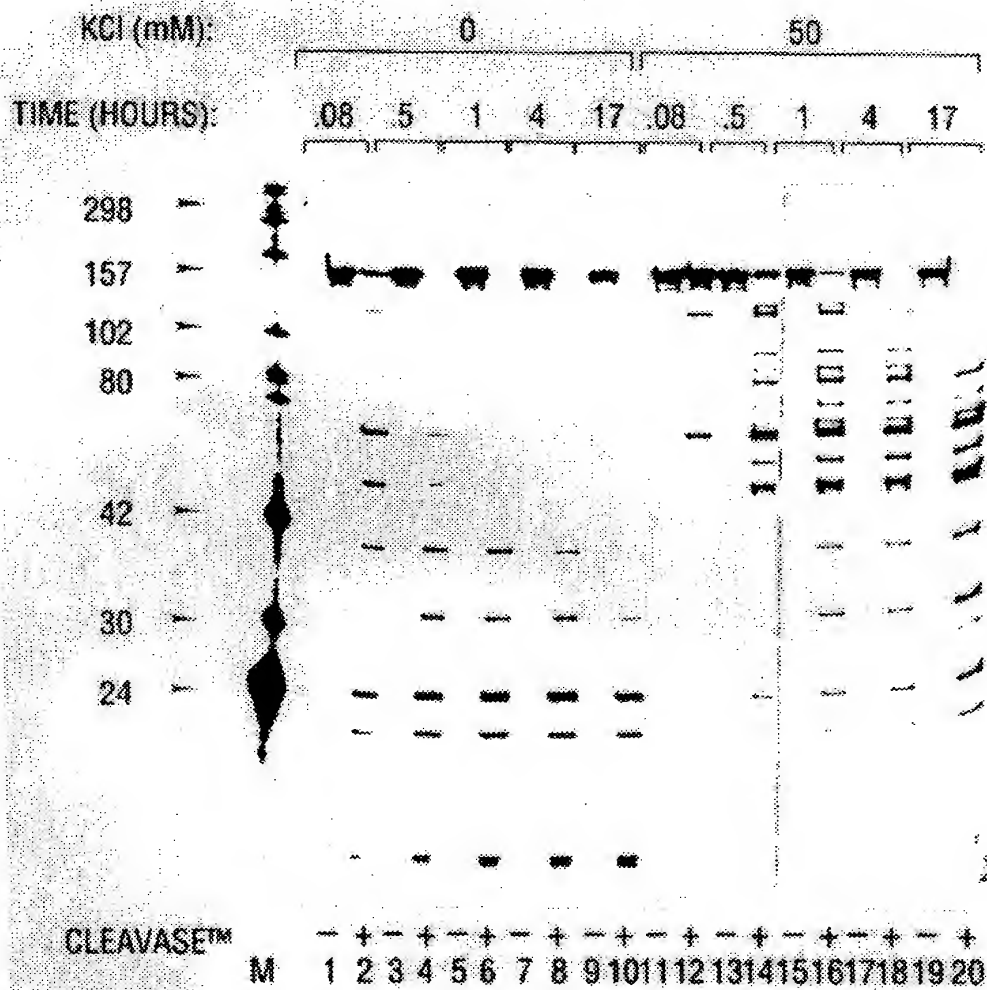


FIG. 55

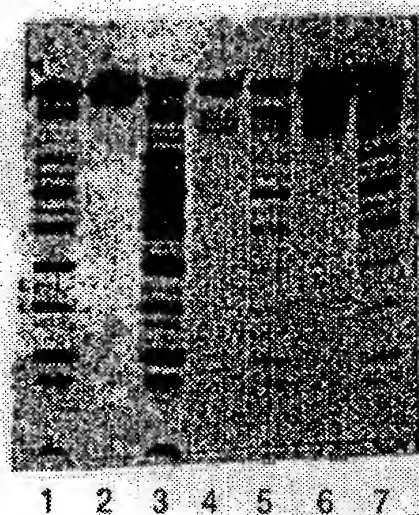


FIG. 56

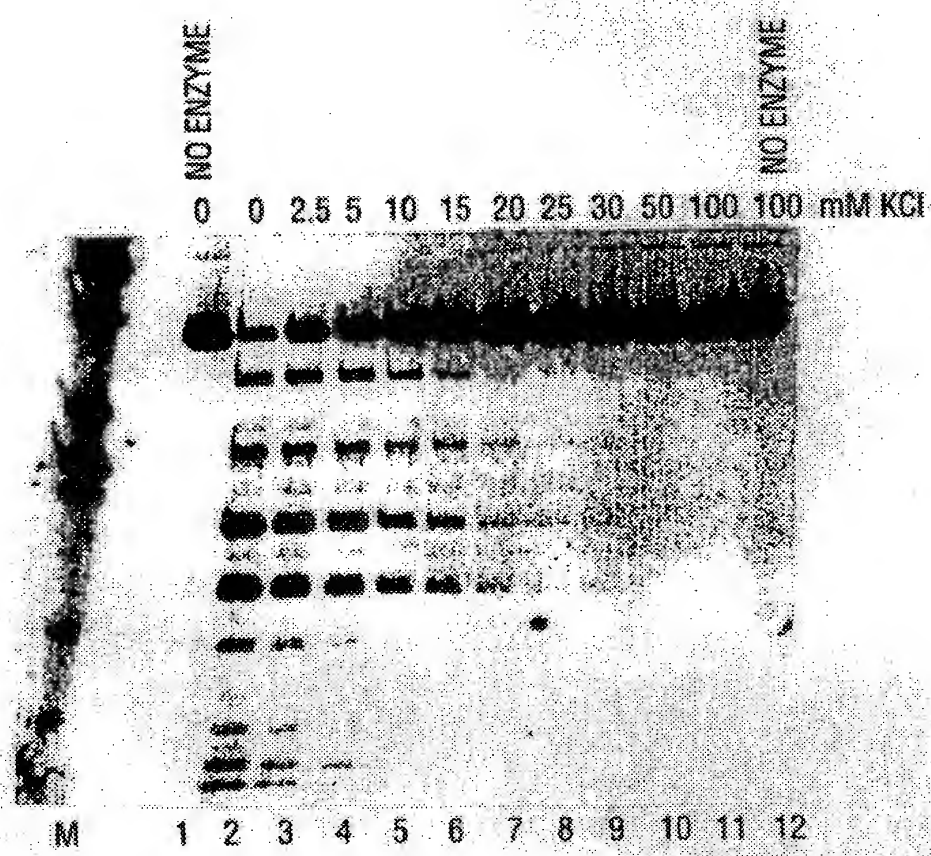


FIG. 57

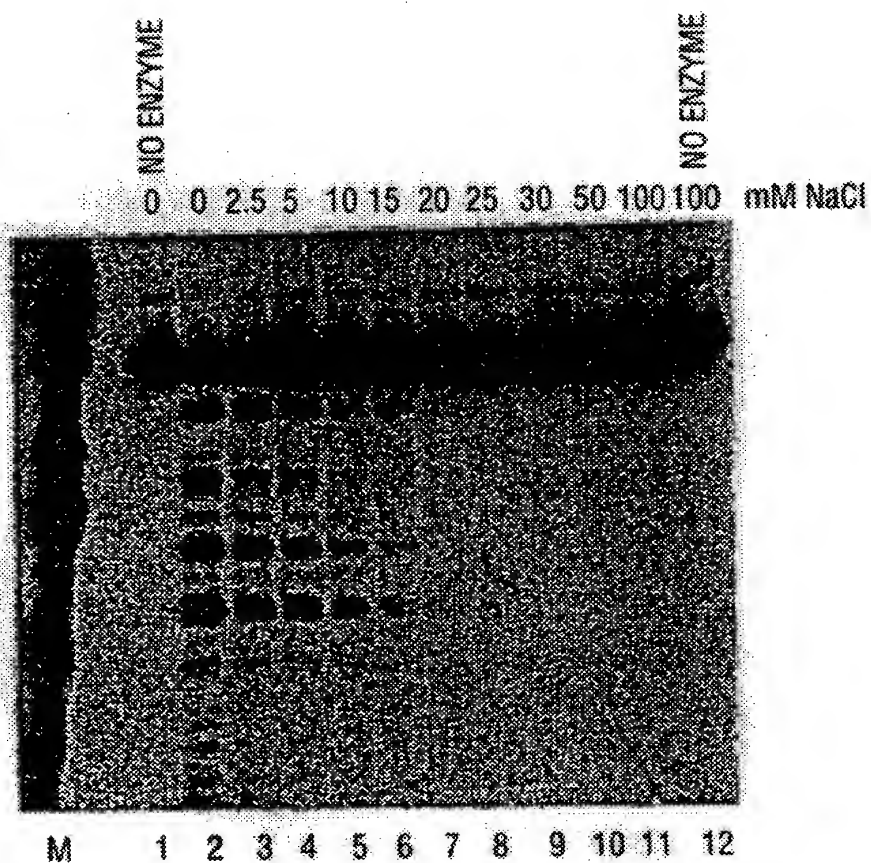


FIG. 58

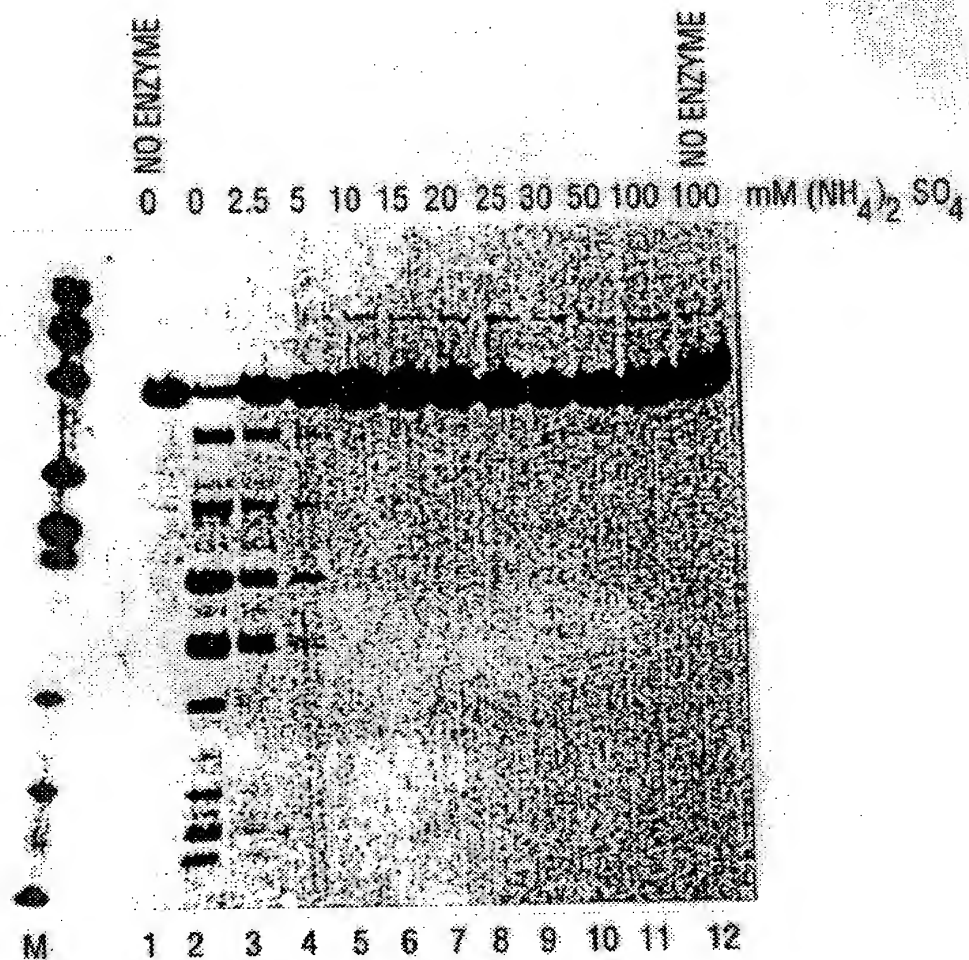


FIG. 59

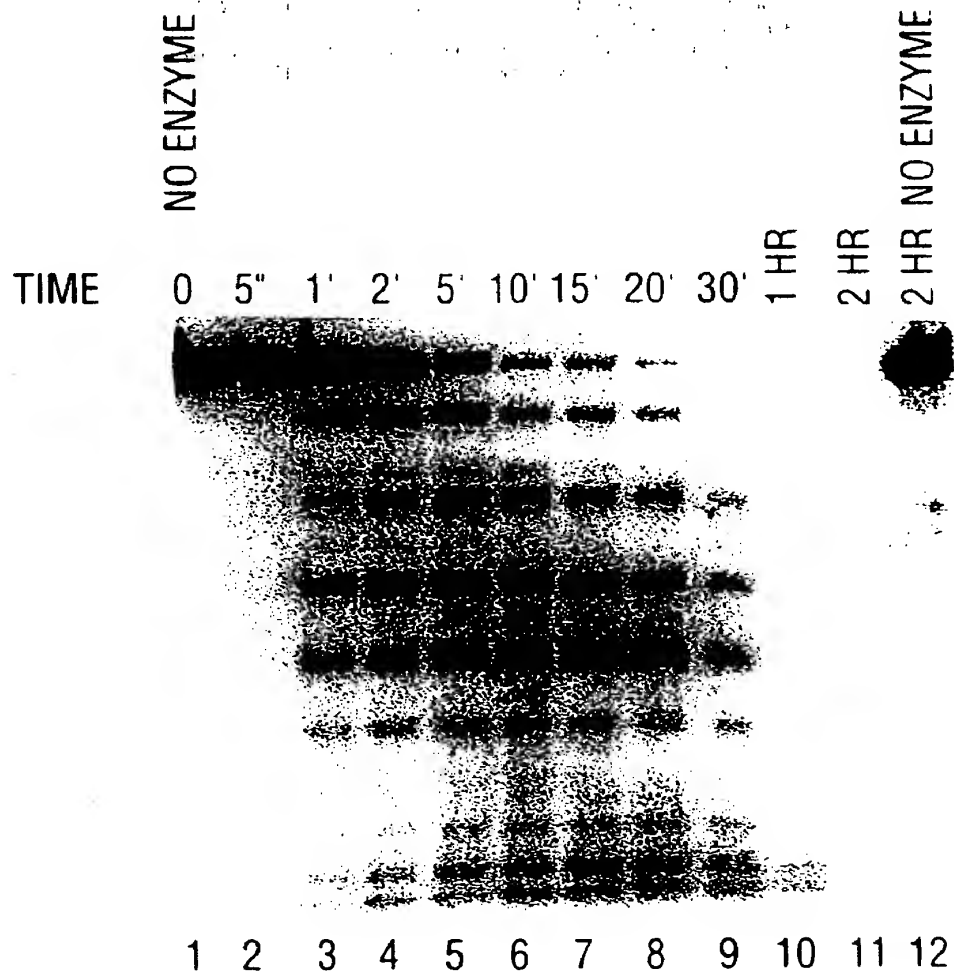


FIG. 60

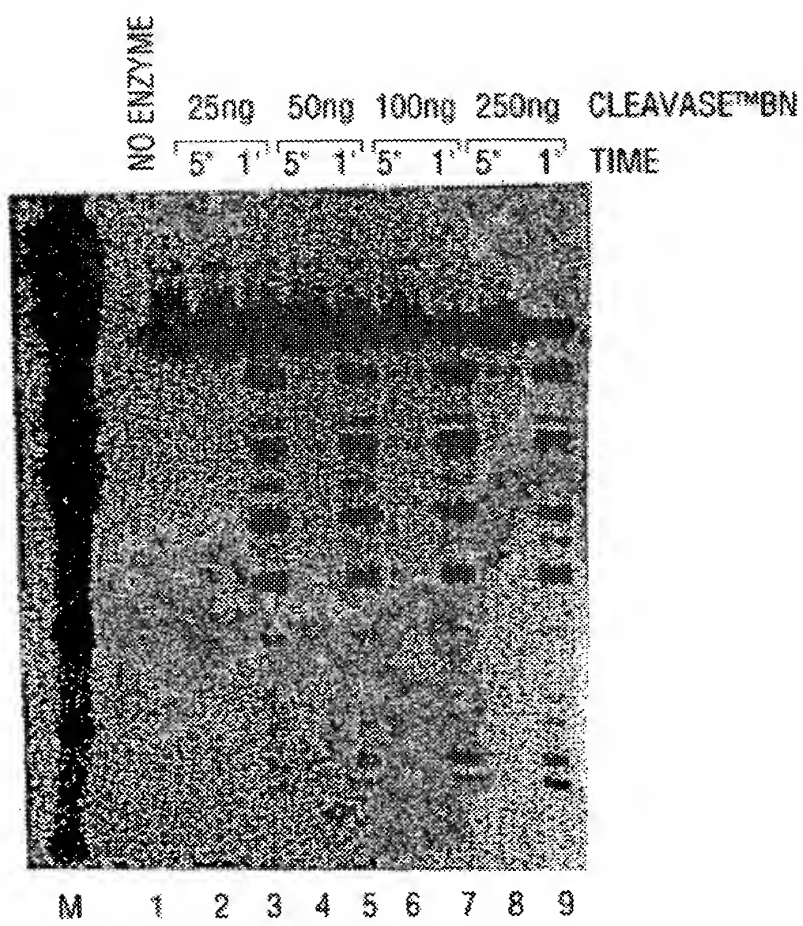


FIG. 61

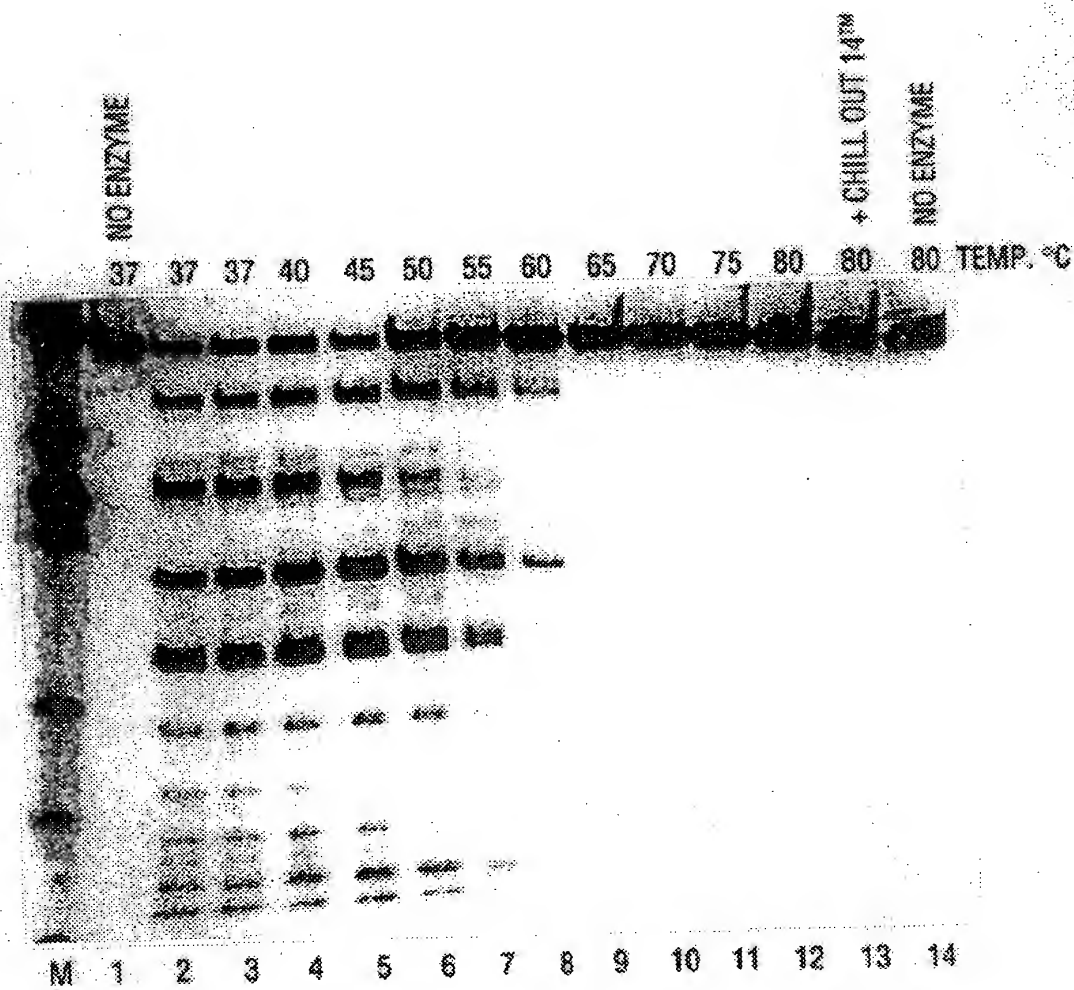


FIG. 62

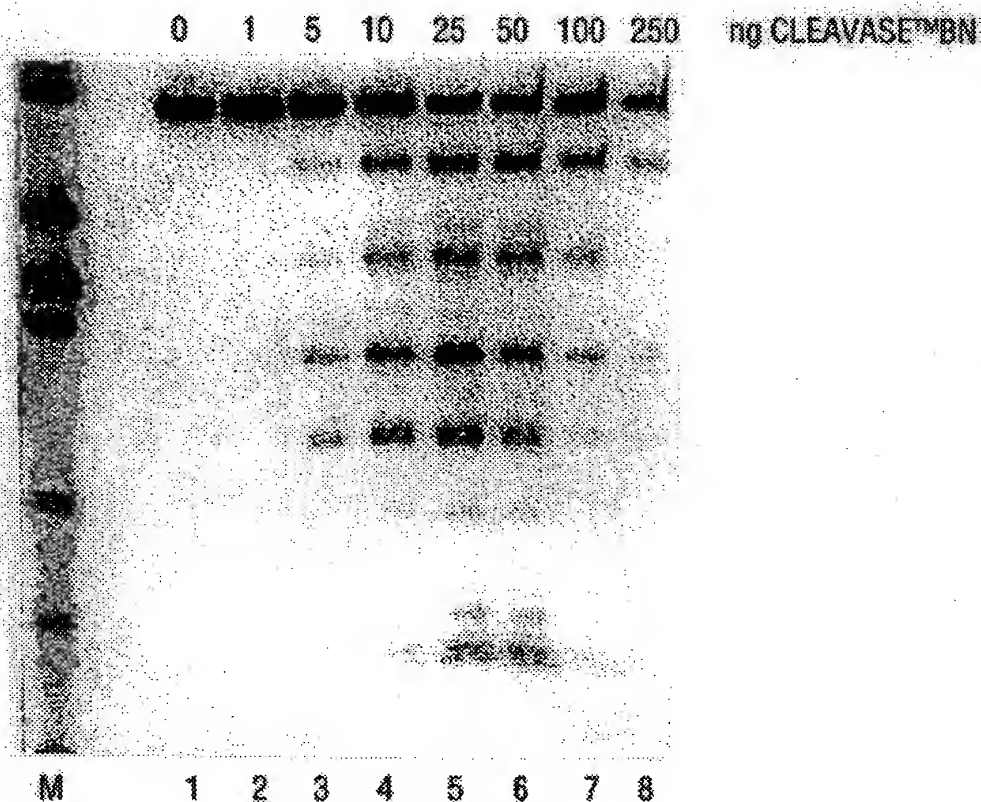


FIG. 63

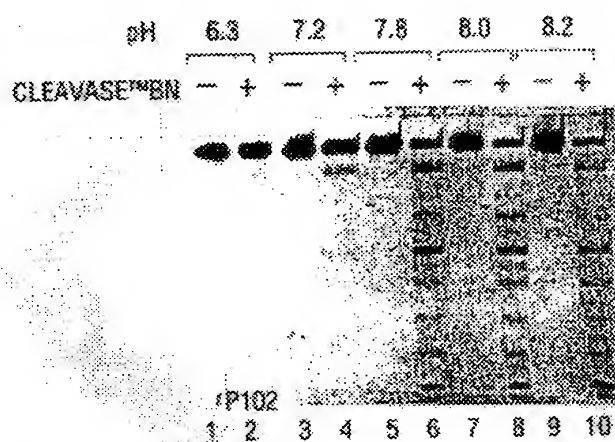
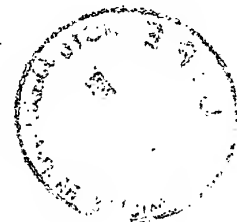


FIG. 64A

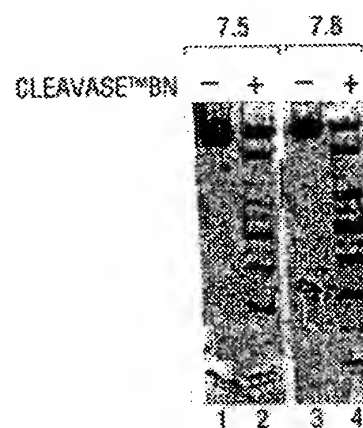


FIG. 64B

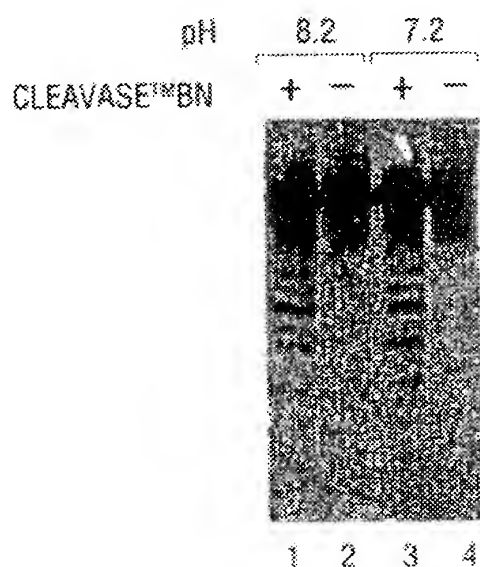


FIG. 65A

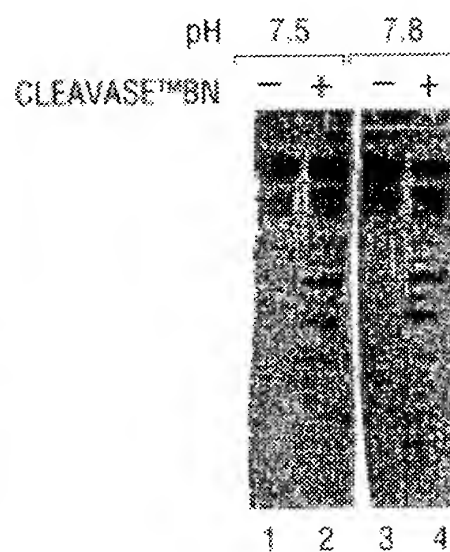


FIG. 65B

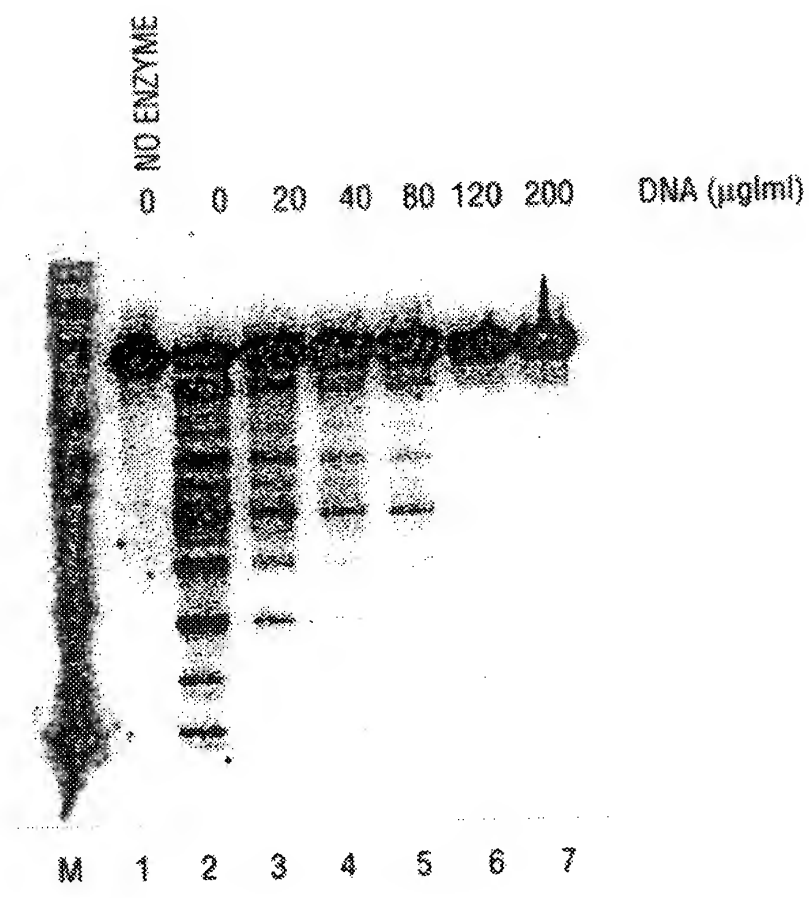


FIG. 66

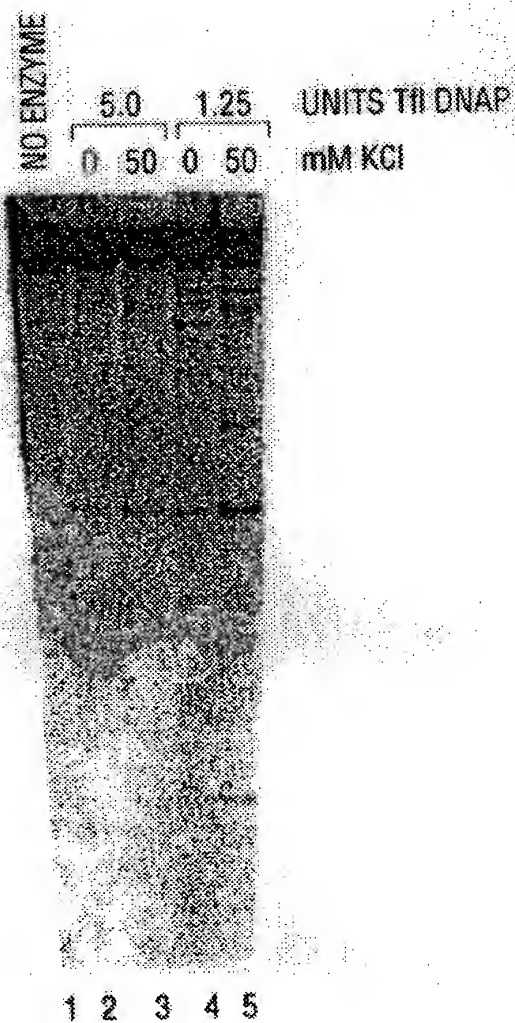


FIG. 67

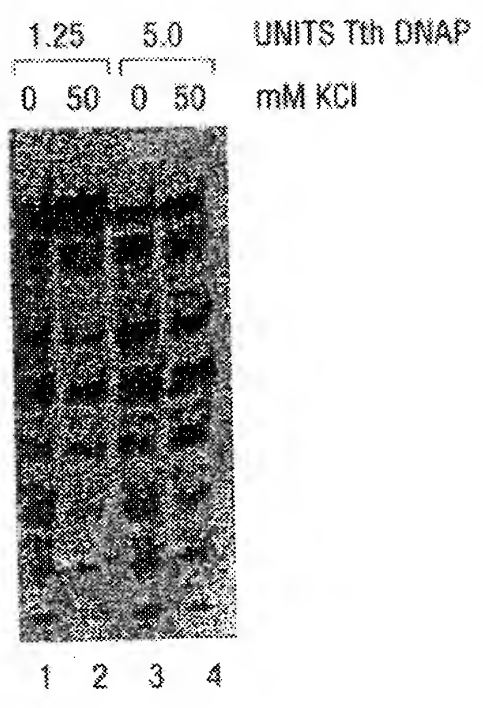


FIG. 68

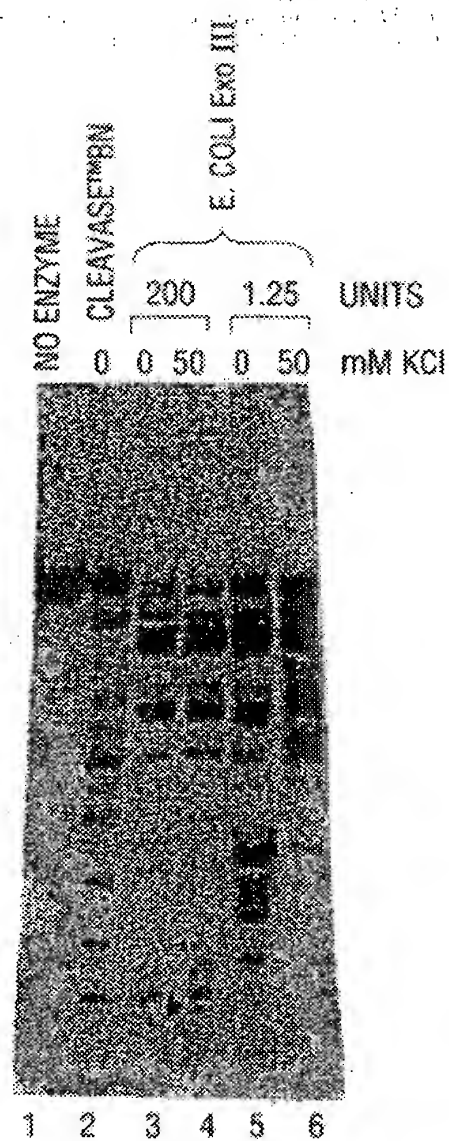


FIG. 69

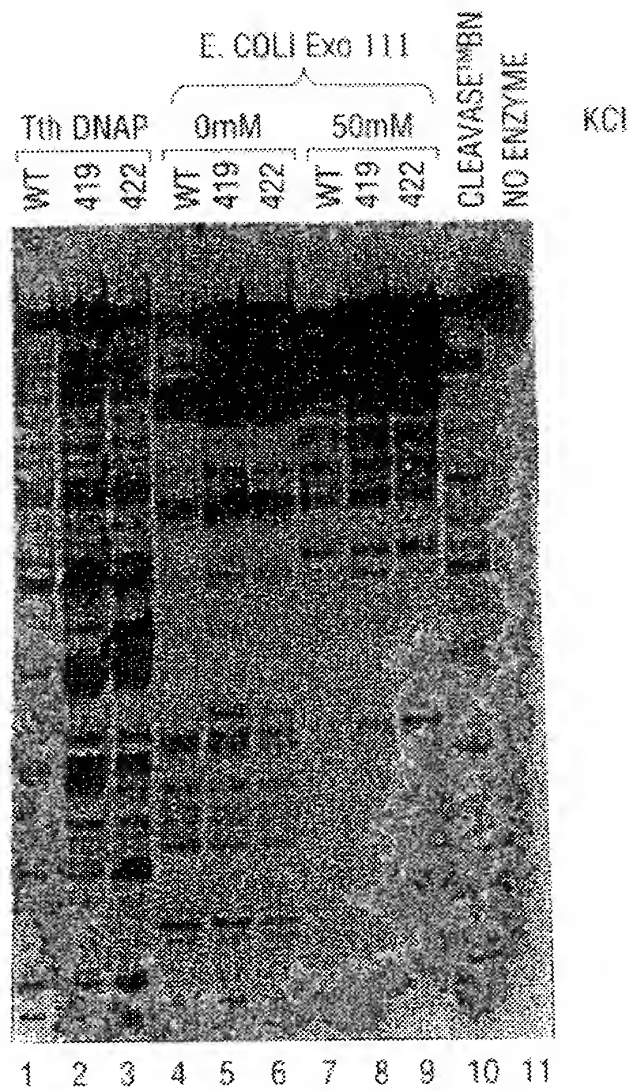
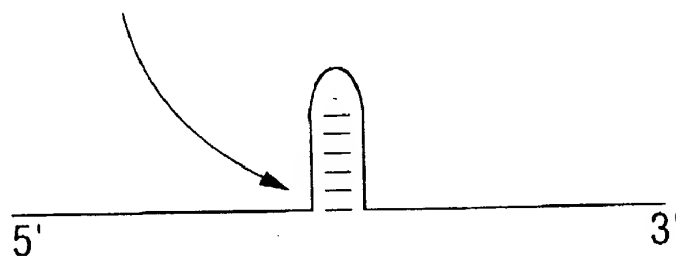


FIG. 70



5' CLEAVAGE SITE



3' CLEAVAGE SITE

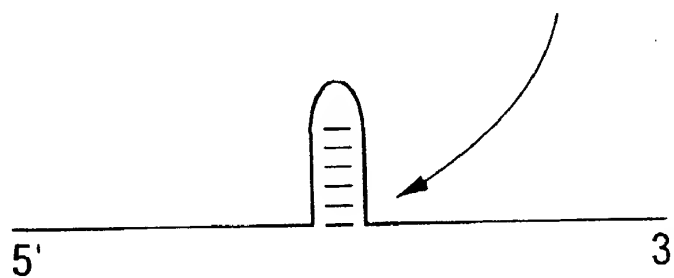


FIG. 71

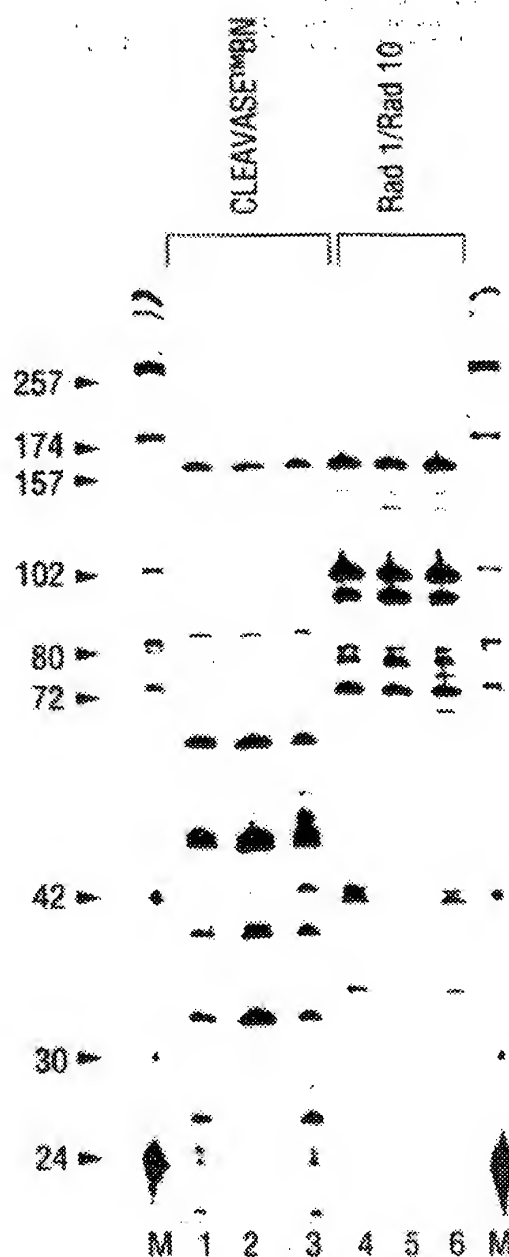


FIG. 72

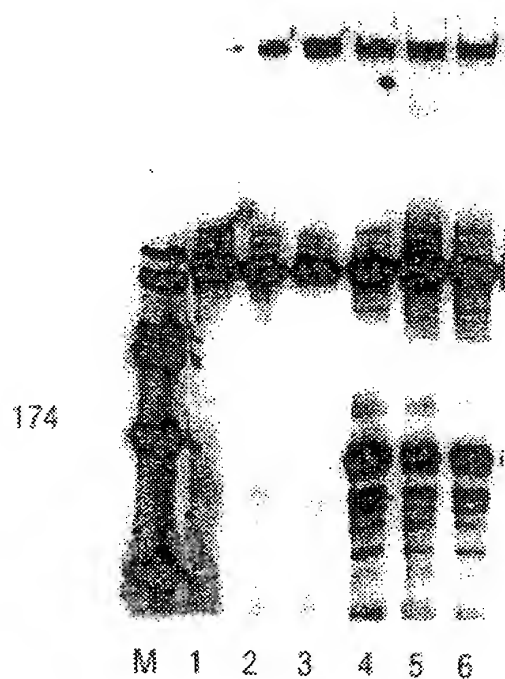


FIG. 73

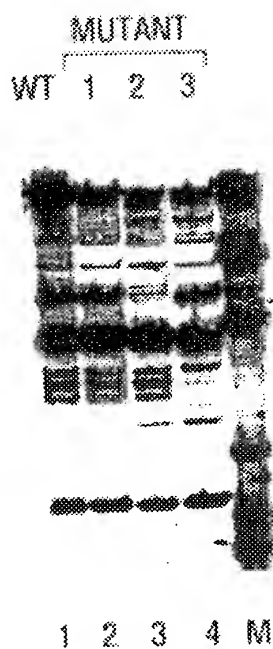


FIG. 74A

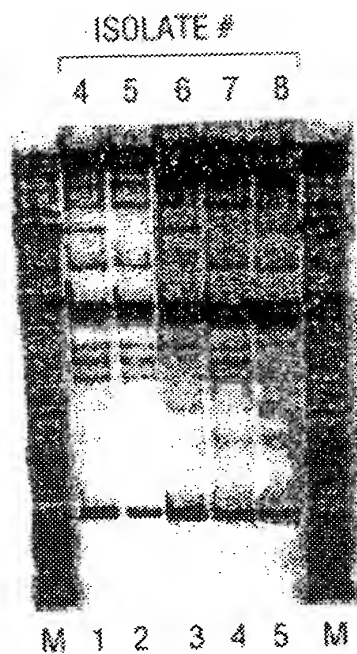


FIG. 74B



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WELFARE

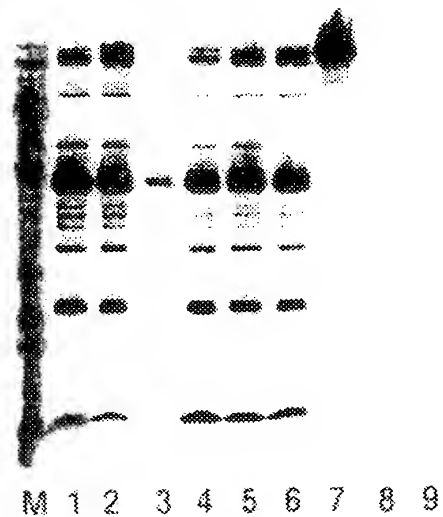


FIG. 75



% OF TOTAL
MUTATIONS

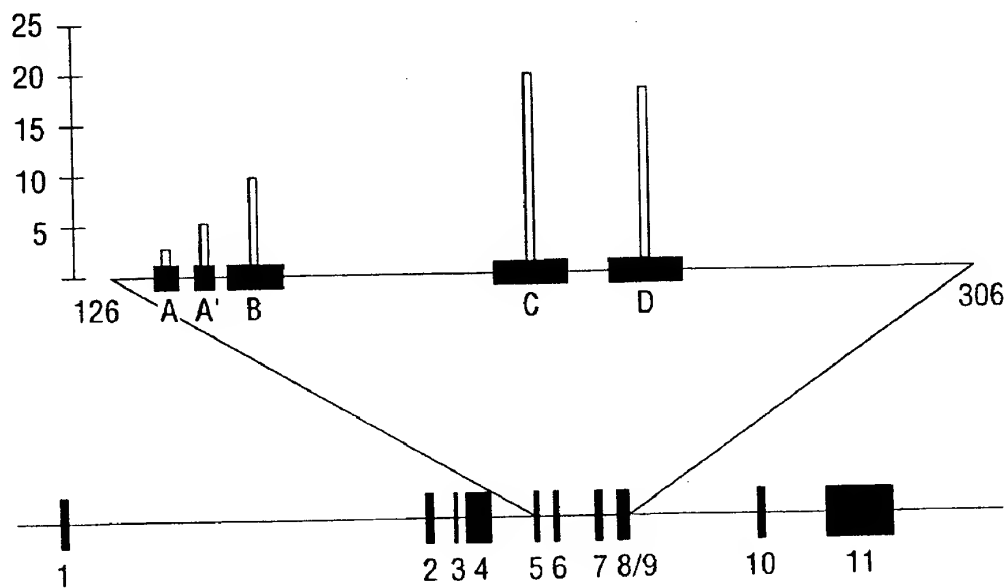


FIG. 76

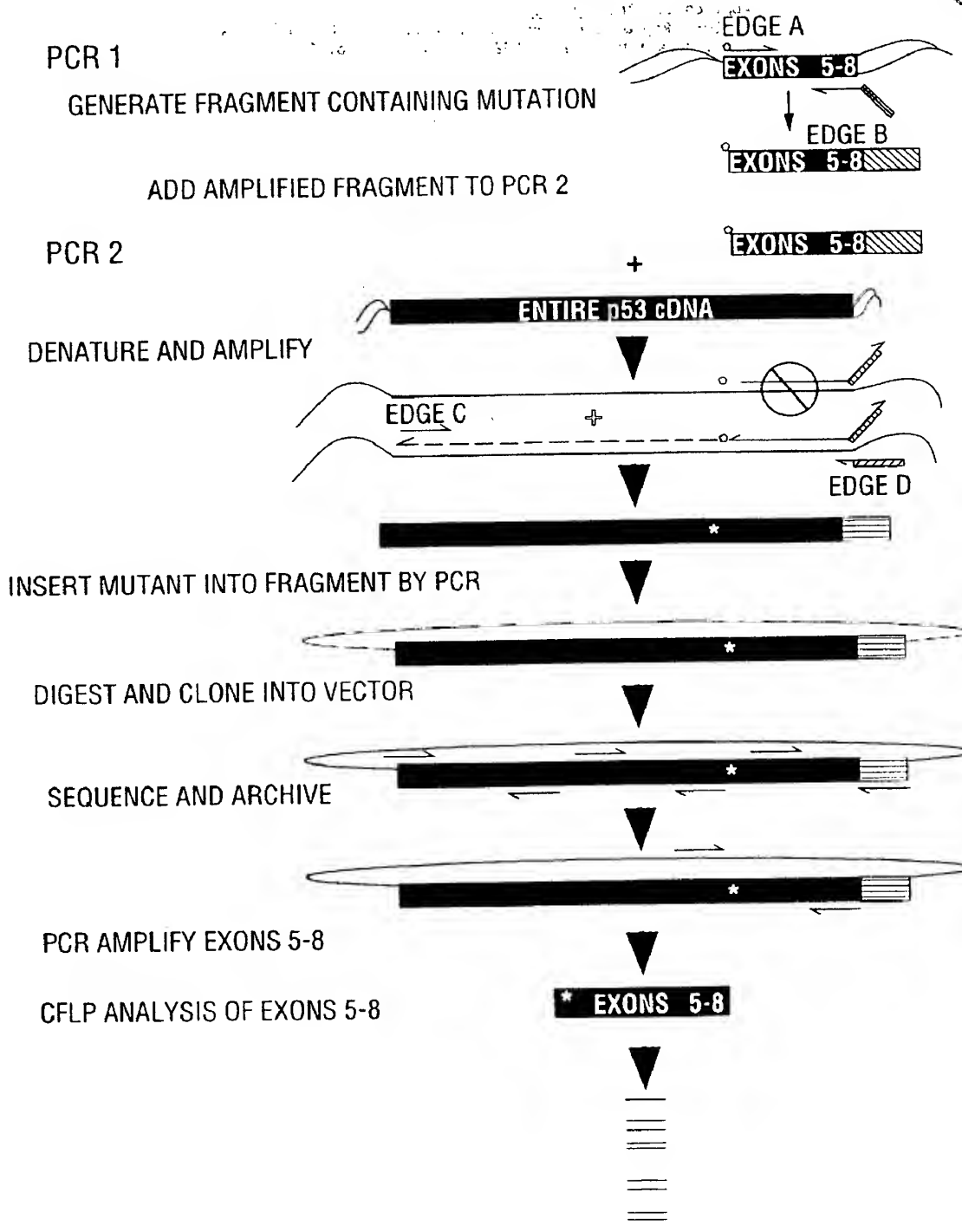


FIG. 77

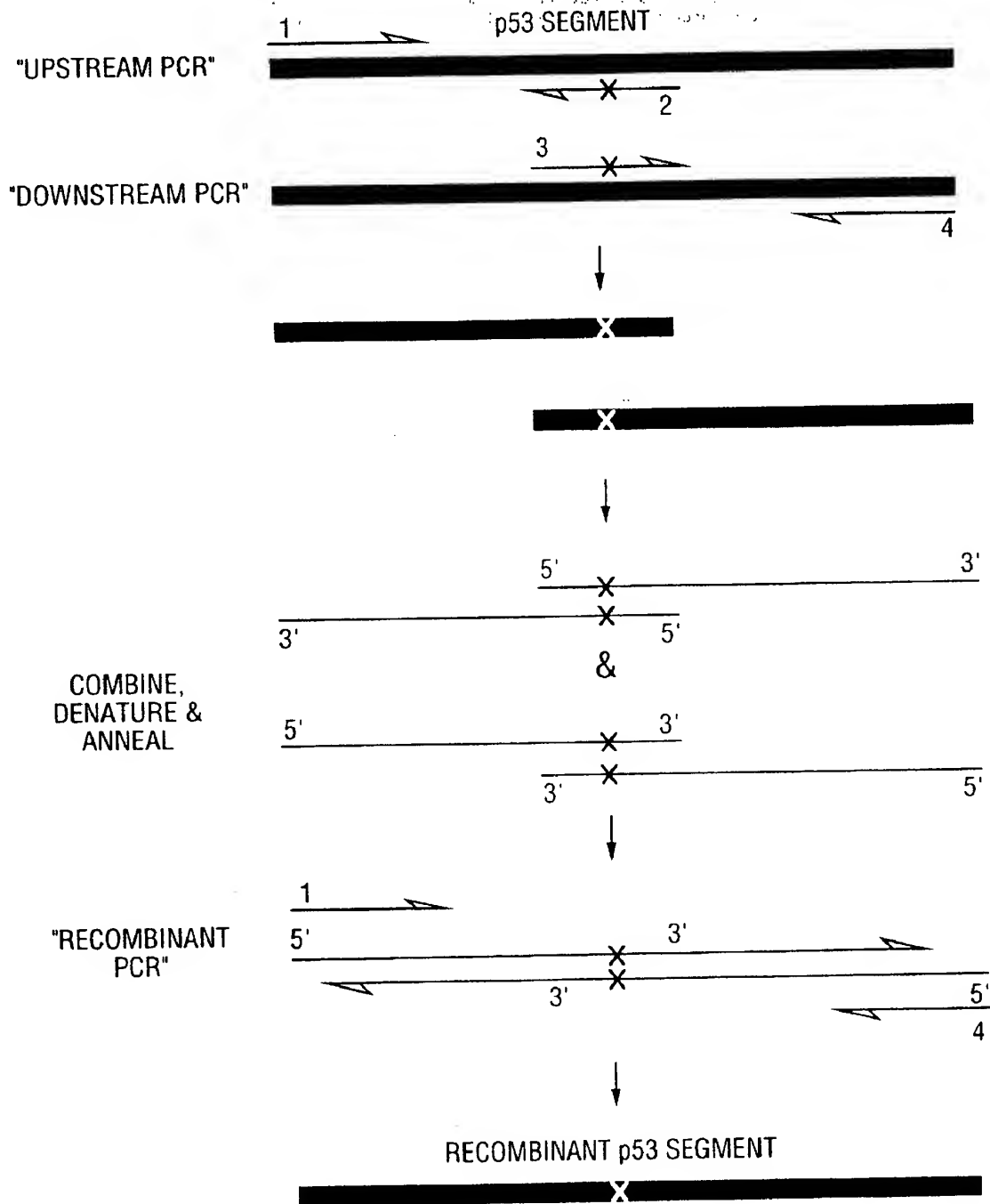


FIG. 78

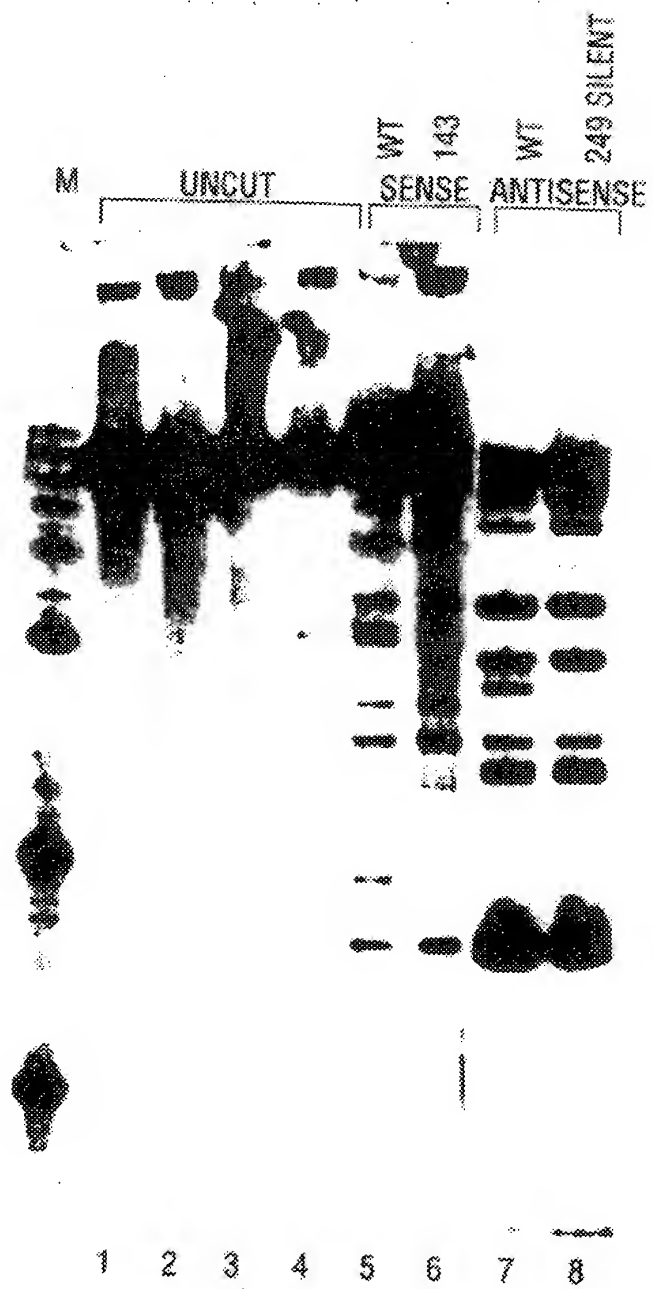


FIG. 79

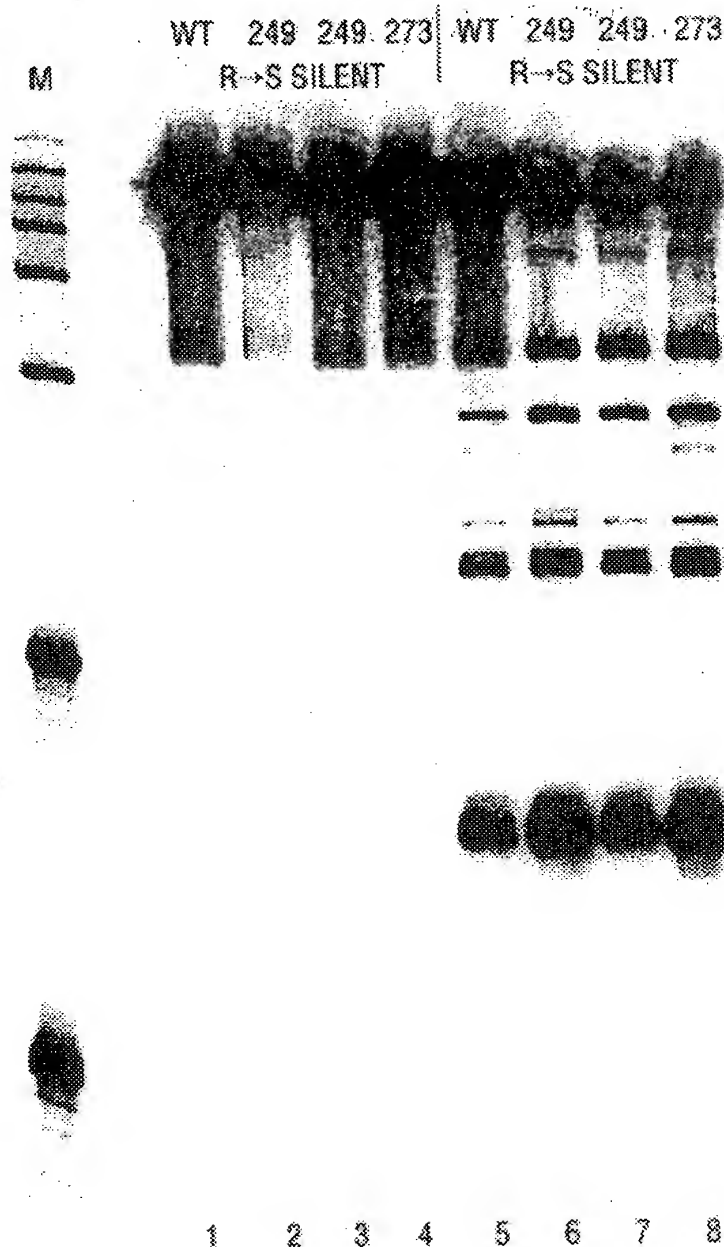


FIG. 80

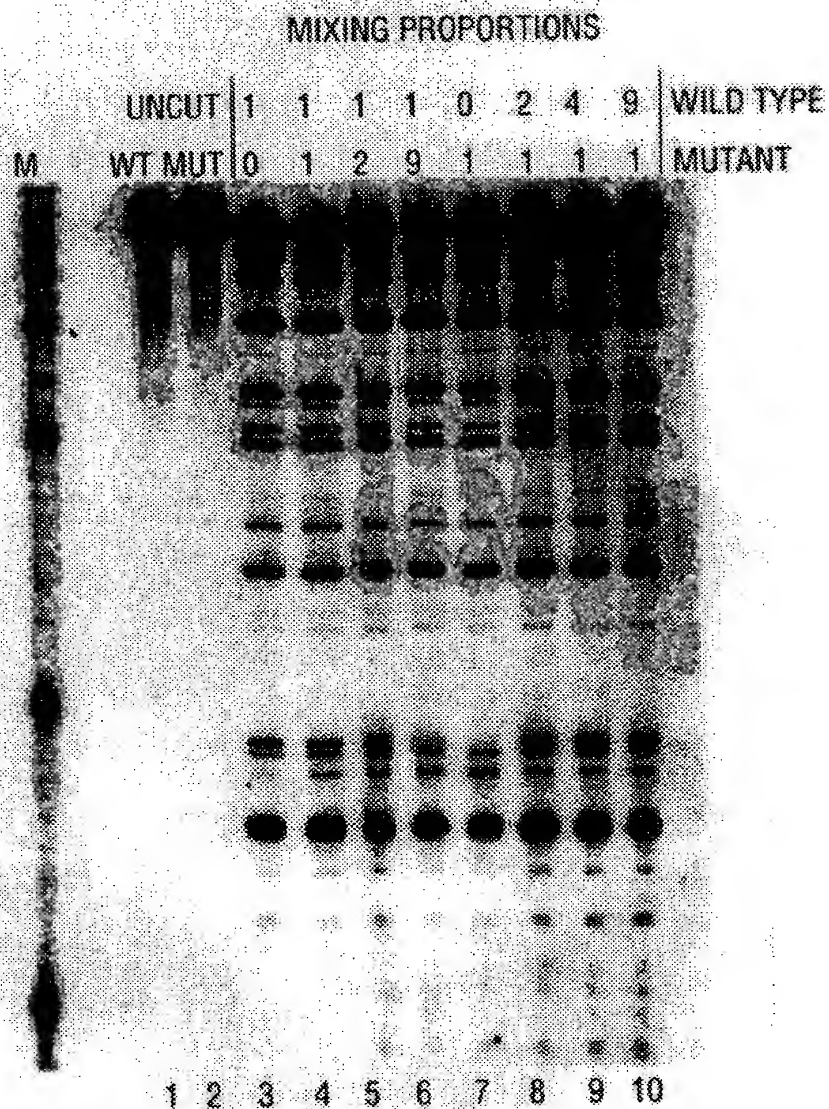


FIG. 81

HCV1.1	(SEQ	ID	N0:121)	1	CTGTCTTTCAC	GCAGAAAGCG	TCTGGCCATG	GCGTTAGTAT	GAGTGTCGTG	50
HCV2.1	(SEQ	ID	N0:122)		CTGTCTTTCAC	GCAGAAAGCG	TCTAGCCATG	GCGTTAGTAT	GAGTGTCGTG	
HCV3.1	(SEQ	ID	N0:123)		CTGTCTTTCAC	GCAGAAAGCG	TCTAGCCATG	GCGTTAGTAT	GAGTGTCGTG	
HCV4.2	(SEQ	ID	N0:124)		CTGTCTTTCAC	GCAGAAAGCG	TCTAGCCATG	GCGTTAGTAT	GAGTGTCGTG	
HCV6.1	(SEQ	ID	N0:125)		CTGTCTTTCAC	GCAGAAAGCG	TCTAGCCATG	GCGTTAGTAT	GAGTGTCGTG	
HCV7.1	(SEQ	ID	N0:126)		CTGTCTTTCAC	GCAGAAAGCG	<u>CTAGCCATG</u>	GCGTTAGTAT	GAGTGTCGTG	
HCV1.1				51	CAGCCTCCAG	GACCCCCCCT	CCCGGGAGAG	CCATAGTGGT	CTGCGGAACC	100
HCV2.1					CAGCCTCCAG	GACCCCCCCT	CCCGGGAGAG	CCATAGTGGT	CTGCGGAACC	
HCV3.1					CAGCCTCCAG	GACCCCCCCT	CCCGGGAGAG	CCATAGTGGT	CTGCGGAACC	
HCV4.2					CAGCCTCCAG	GACCCCCCCT	CCCGGGAGAG	CCATAGTGGT	CTGCGGAACC	
HCV6.1					CAGCCTCCAG	GACCCCCCCT	CCCGGGAGAG	CCATAGTGGT	CTGCGGAACC	
HCV7.1					CAGCCTCCAG	GACCCCCCCT	CCCGGGAGAG	CCATAGTGGT	CTGCGGAACC	
HCV1.1				101	GGTGAGTACA	CCGGAATTGC	CAGGACGACC	GGGTCCTTTC	TTGGAT- <u>AAA</u>	150
HCV2.1					GGTGAGTACA	CCGGAATTGC	CAGGACGACC	GGGTCCTTTC	TTGGAT- <u>CAA</u>	
HCV3.1					GGTGAGTACA	CCGGAATTGC	CAGGACGACC	GGGTCCTTTC	TTGGAT- <u>CAA</u>	
HCV4.2					GGTGAGTACA	CCGGAATTGC	CAGGACGACC	GGGTCCTTTC	<u>GTGGATGIAA</u>	
HCV6.1					GGTGAGTACA	CCGGAATTGC	<u>CGGGAAGACT</u>	GGGTCCTTTC	TTGGAT- <u>AAA</u>	
HCV7.1					GGTGAGTACA	CCGGAATCGC	<u>IGGGTIGACC</u>	GGGTCCTTTC	TTGGAG- <u>CAA</u>	

FIG. 82A



HCV1.1	151	CCCGCTCAAT	GCCTGGAGAT	TTGGGCGGTGC	CCCCGCAAGA	CTGCTAGCCG	200
HCV2.1		CCCGCTCAAT	GCCTGGAGAT	TTGGGCGGTGC	CCCCGCAAGA	CTGCTAGCCG	
HCV3.1		CCCGCTCAAT	GCCTGGAGAT	TTGGGCGGTGC	CCCCGCGAGA	CTGCTAGCCG	
HCV4.2		CCCGCTCAAT	GCCTGGAGAT	TTGGGCGGTGC	CCCCGCAAGA	CTGCTAGCCG	
HCV6.1		CCCACTCIAT	GCCGGGCCAT	TTGGGCGGTGC	CCCCGCAAGA	CTGCTAGCCG	
HCV7.1		CCCGCTCAAT	ACCCAGAAAT	TTGGGCGGTGC	CCCCGCGAGA	ICACTAGCCG	
HCV1.1	201	AGTAGTGTTG	GGTCGCGAAA	GGCCTTGTGG	TACTGCCTGA	TAGGGTGCTT	250
HCV2.1		AGTAGTGTTG	GGTCGCGAAA	GGCCTTGTGG	TACTGCCTGA	TAGGGTGCTT	
HCV3.1		AGTAGTGTTG	GGTCGCGAAA	GGCCTTGTGG	TACTGCCTGA	TAGGGTGCTT	
HCV4.2		AGTAGTGTTG	GGTCGCGAAA	GGCCTTGTGG	TACTGCCTGA	TAGGGTGCTT	
HCV6.1		AGTAGCGTTG	GGTIGCGAAA	GGCCTTGTGG	TACTGCCTGA	TAGGGTGCTT	
HCV7.1		AGTAGTGTTG	GGTCGCGAAA	GGCCTTGTGG	TACTGCCTGA	TAGGGTGCTT	
HCV1.1	251	GCGAGTGCCC	GCGGAGGTCT	CGTAGACCGT	GC	282	
HCV2.1		GCGAGTGCCC	GCGGAGGTCT	CGTAGACCGT	GC		
HCV3.1		GCGAGTGCCC	GCGGAGGTCT	CGTAGACCGT	GC		
HCV4.2		GCGAGTGCCC	GCGGAGGTCT	CGTAGACCGT	GC		
HCV6.1		GCGAGTACCC	GCGGAGGTCT	CGTAGACCGT	GC		
HCV7.1		GCGAGTGCCC	GCGGAGGTCT	CGTAGACCGT	GC		

FIG. 82B



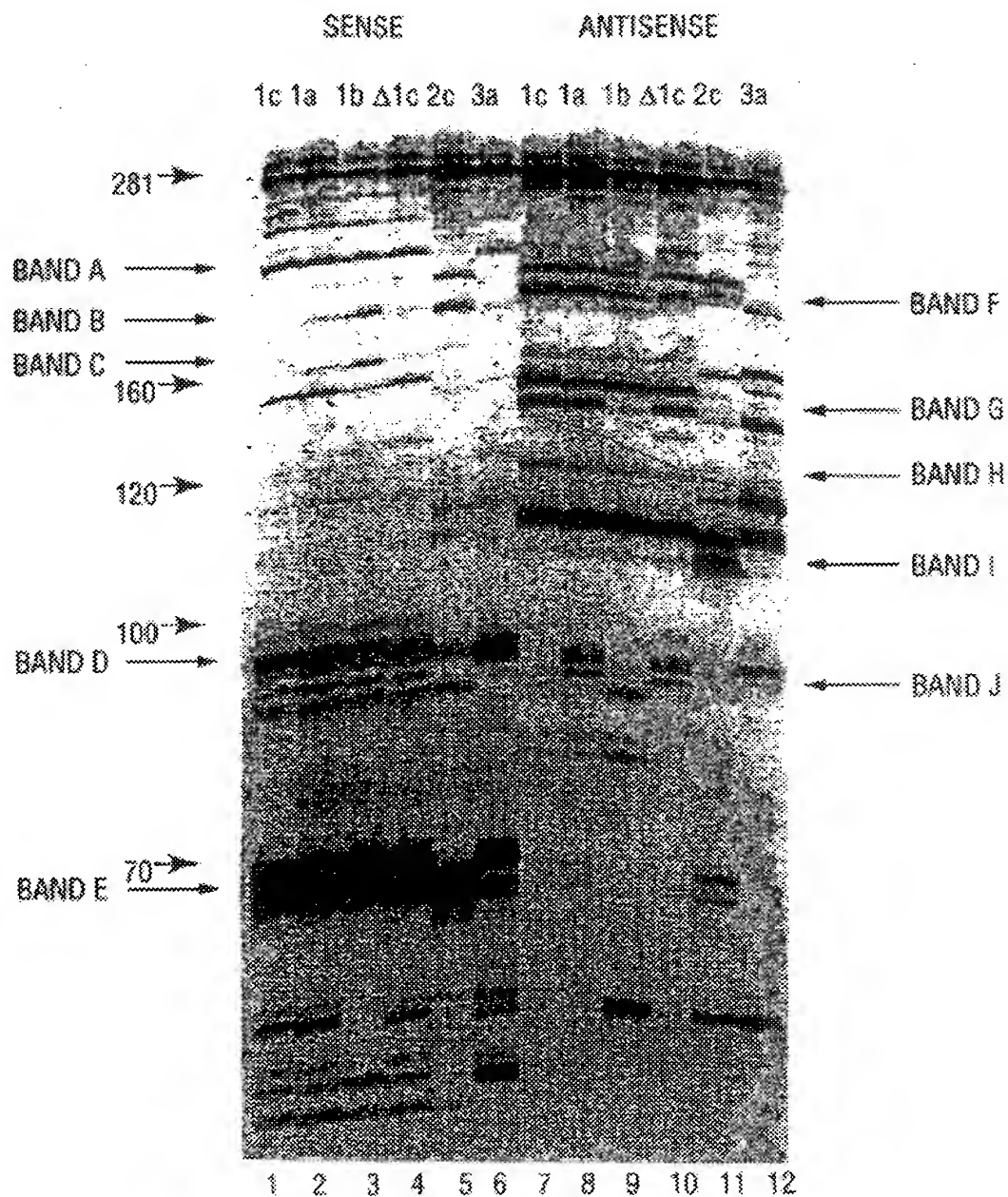


FIG. 83

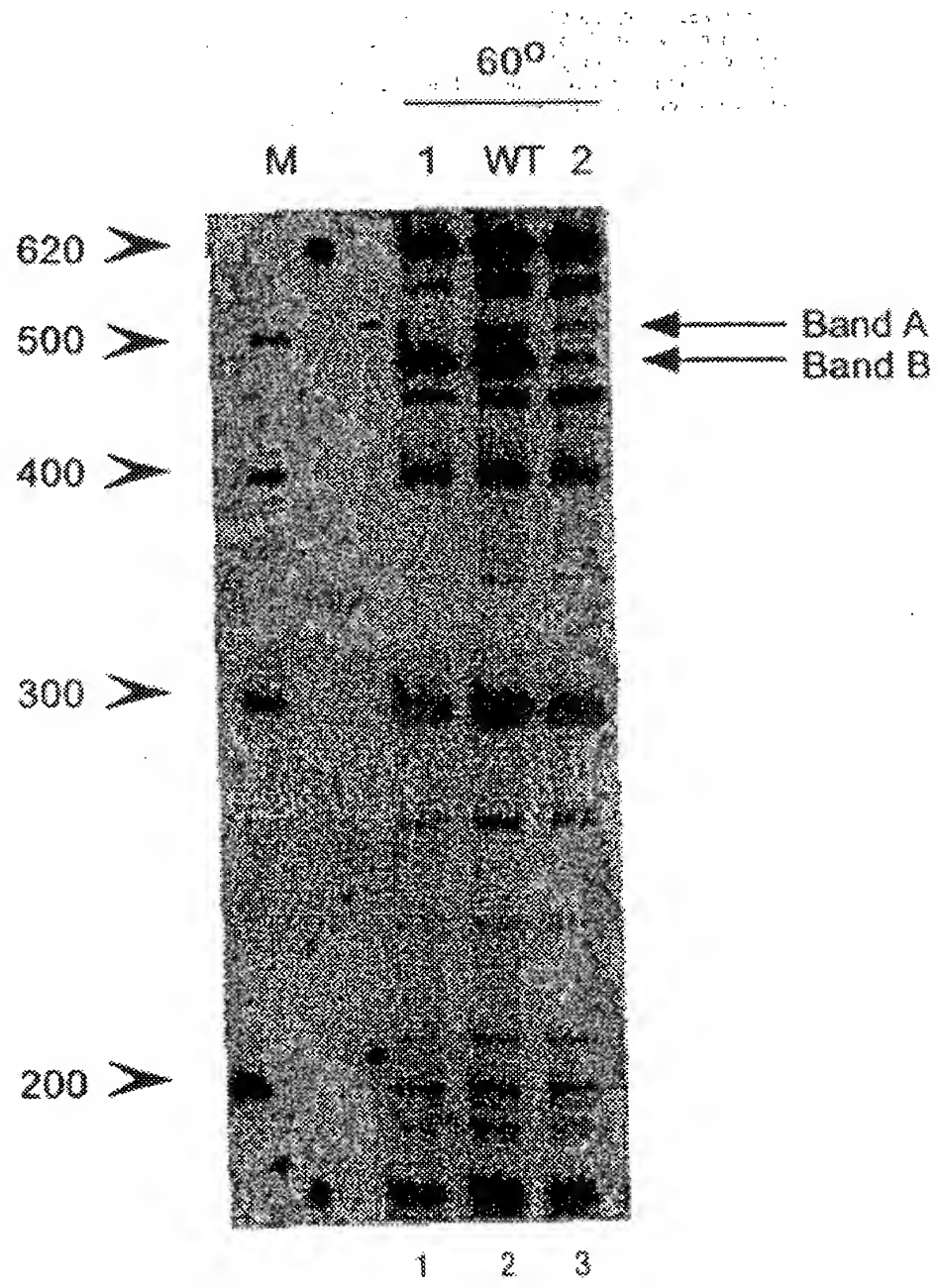


FIG. 84

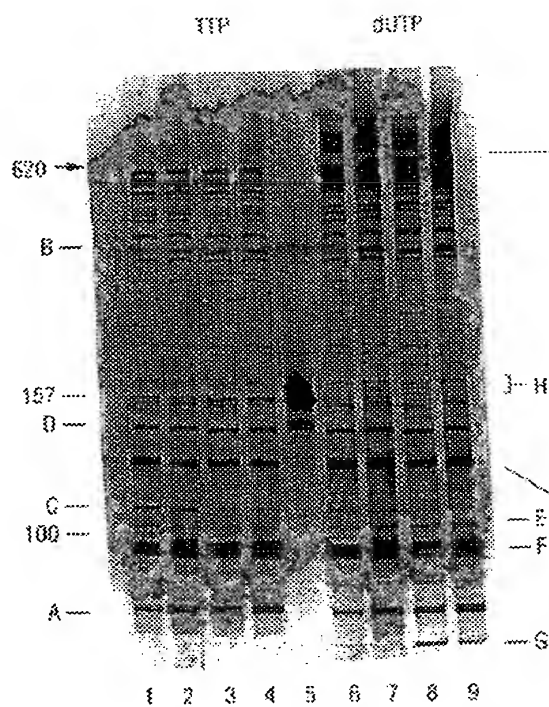


FIG. 85A

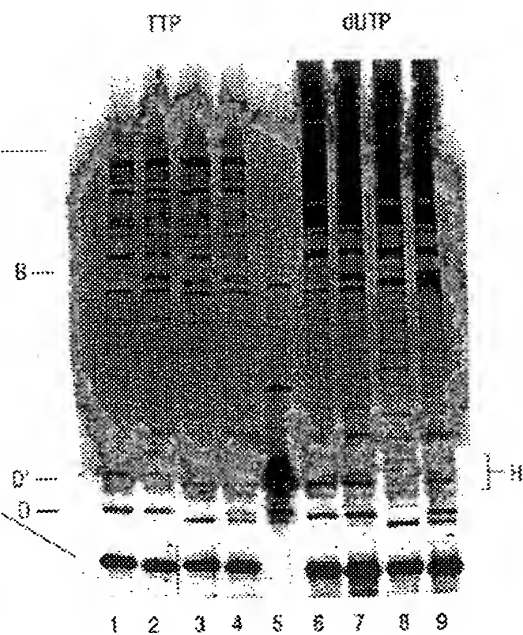


FIG. 85B

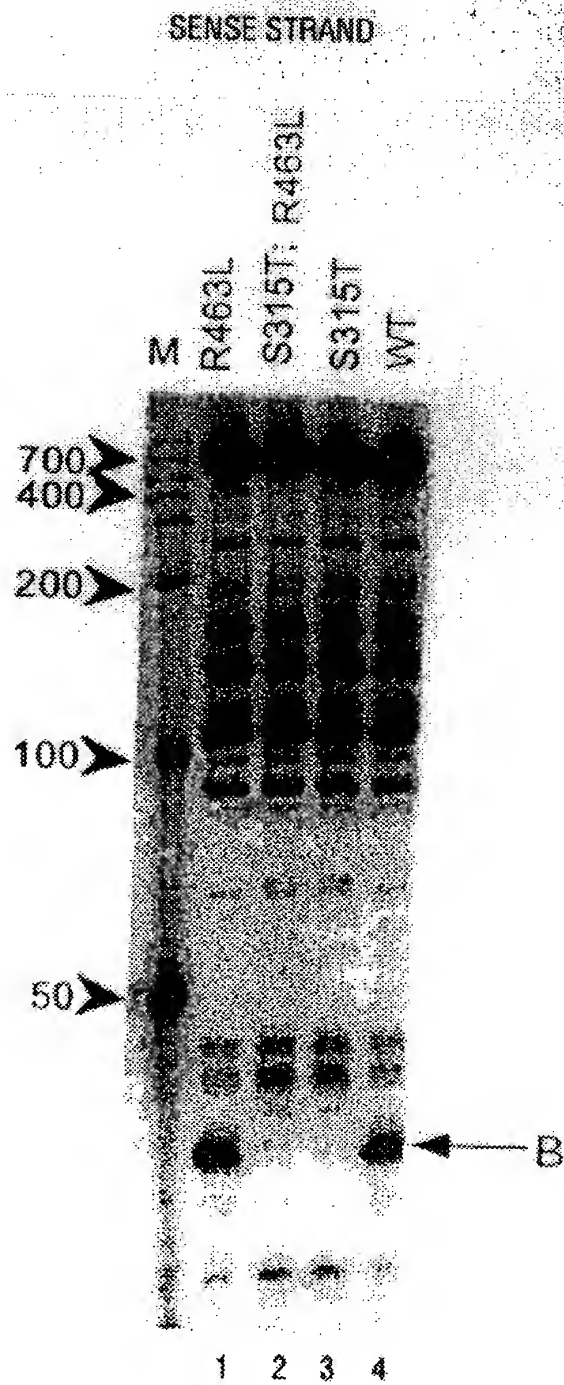


FIG. 86

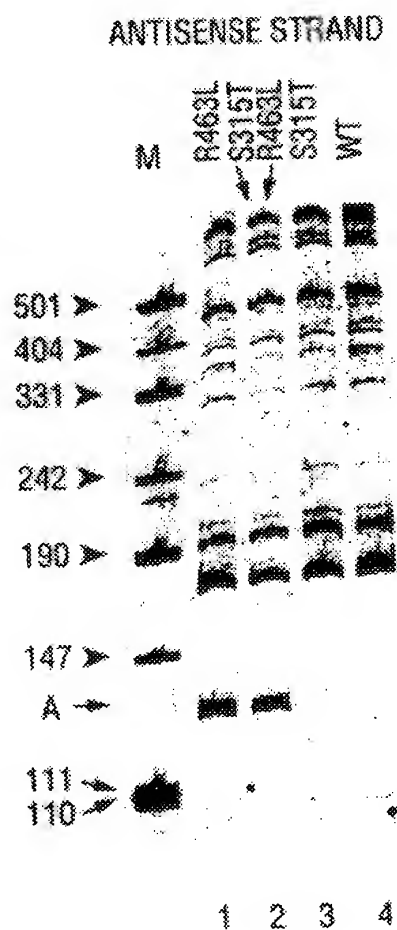
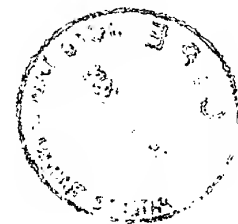


FIG. 87

1638

10 20 30 40 50 60
 AGA GTTTGATCCT GGCTCAG
 AAATTGAAGA GTTIGATCAT GGCTCAGATT GAACGCTGGC GGCAGGCCTA ACACATGCAA
 TTTAACTTCT CAAACTAGTA CCGAGTCTAA CTTGCGACCG CCGTCCGGAT TGTGTACGTT

ER10

70 80 90 100 110 120
 GTCGAACGGT AACAGGAAGA AGCTTGCTTC TTTGCTGACG AGTGGCGGAC GGTGAGTAA
 CAGCTTGCCA TTGTCCTTCT TCGAACGAAG AACGACTGC TCACCGCCTG CCCACTCATT
 GCGCGAC GGTGAGTAA

130 140 150 160 170 180
 TGTCTGGGAA ACTGCCTGAT GGAGGGGGAT AACTACTGGA AACGGTAGCT AATACCGCAT
 ACAGACCCCT TGACGGACTA CCTCCCCCTA TTGATGACCT TTGCCATCGA TTATGGCGTA

190 200 210 220 230 240
 AACGTCGCAA GACCAAAGAG GGGGACCTTC GGGCCTCTTG CCATCGGATG TGCCCCAGATG
 TTGCAGCGTT CTGTTTCTC CCCCTGGAAG CCCGGAGAAC GGAGCCTAC ACGGGTCTAC

250 260 270 280 290 300
 GGATTAGCTA GTAGGTGGGG TAACGGCTCA CCTAGGCGAC GATCCCTAGC TGGTCTGAGA
 CCTAATCGAT CATCCACCCC ATTGCCGAGT GGATCCGCTG CTAGGGATCG ACCAGACTCT

310 320 330 340 350 360
 GGATGACCCAG CCACACTGGA ACTGAGACAC GTTCCAGACT CCTACGGGAG GCAGCAGTGG
 CCTACTGGTC GGTGTGACCT TGACTCTGTG CCAGGTCIGA GGATGCCCTC CGTCGTCACC
 TGA GGATGCCCTC CGTCGTC

1659

FIG. 88A





370 GGAATATTGC 380 ACAATGGGCG 390 CAAGCCTGAT 400 GCAGCCATGC 410 CGCGTGTATG 420 AAGAAGGCCT
CCTTATAACG TGTTACCCGC GTTCGGACTA CGTCGGTACG GCGCACATAC TTCTTCCGGA

430 TCGGGTTGTA 440 AAGTACTTTC 450 AGCGGGGAGG 460 AAGGGAGTAA 470 AGTTAATACC 480 TTTGCTCATT
AGCCCAACAT TTCATGAAAG TCGCCCTCTC TTCCCTCATT TCAATTATGG AACCGAGTAA

490 GACGTTACCC 500 GCAGAAGAAG 510 CACCGGCTAA 520 CTCCGTGCCA 530 GCAGCCGCGG 540 TAATACGGAG
CTGCAATGGG CGTCTTCTC GTGGCCGATT GAGGCACGGT CGTCGGCGCC ATTATGCCTC

550 GGTGCAAGCG 560 TTAATCGGAA 570 TTAAGTGGCG 580 TAAAGCGCAC 590 GCAGGCGGTT 600 TGTTAAGTCA
CCACGTTTCG AATTAGCCTT AATGACCCGC ATTTCGCGTG CGTCCGCCAA ACAATTTCAGT

610 GATGTGAAAT 620 CCCCGGGCTC 630 AACCTGGGAA 640 CTGCATCTGA 650 TACTGGCAAG 660 CTTGAGTCTC
CTACACTTTA GGGGCCCCGAG TTGGACCCCTT GACGTAGACT ATGACCGTTC GAACTCAGAG

670 GTAGAGGGG 680 GTAGAATTCC 690 AGGTGTAGCG 700 GTGAAATGCG 710 TAGAGATCTC 720 GAGGAATACC
CATCTCCCCC CATCTTAAGG TCCACATCGC CACTTTACGC ATCTCTAGAC CTCCTTATGG

730 GGTGGCGAAG 740 GCGGCCCCCT 750 GGACGAAGAC 760 TGACGCTCAG 770 GTGCGAAAGC 780 GTGGGGAGCA
CCACCGCTTC CGCCGGGGGA CCTGCTTCTG ACTGCGAGTC CACGCTTTTCG CACCCCTCGT

FIG. 88B



790 800 810 820 830 840
AACAGGATTA GATACCCTGG TAGTCCACGC CGTAAACGAT GTCGACTTGG AGGTTGTGCC
TTGTCCTAAT CTATGGGACC ATCAGGTGCG GCATTTGCTA CAGCTGAACC TCCAACACGG
850 860 870 880 890 900
CTTGAGGCGT GGCTTCCGGA GCTAACGCGT TAAGTCGACC GCCTGGGGAG TACGGCCGCA
GAACTCCGCA CCGAAGGCCT CGATTGCGCA ATTCAGCTGG CGGACCCCTC ATGCCGGCGT
910 920 930 940 950 960
AGGTTAAAC TCAAATGAAT TGACGGGGGC CCGCACAAAGC GGTGGAGCAT GTGGTTTAAT
TCCAATTTG AGTTTACTTA ACTGCCCCCG GCGTGTTGCG CCACCTCGTA CACCAAATTA
970 980 990 1000 1010 1020
TCGATGCAAC GCGAAGAACC TTACCTGGTC TTGACATCCA CGGAAGTTTT CAGAGATGAG
AGCTACGTTG CGCTTCTTGG AATGGACCAG AACTGTAGGT GCCTTCAAAA GTCTCTACTC
1030 1040 1050 1060 1070 1080
AATGTGCCCT CGGGAACCGT GAGACAGGTG CTGCATGGCT GTCGTCAGCT CGTGTGTGA
TTACACGGAA GCCCTTGGCA CTCTGTCCAC GACGTACCGA CAGCAGTCGA GCACAACACT
1090 1100 1110 1120 1130 1140
GC AACGAGCGCA ACCC
AATGTTGGT TAAGTCCCGC AACGAGCGCA ACCCTTATCC TTTGTTGCCA GCGGTCCGGC
TTACAACCCA ATTCAGGGCG TTGCTCGCGT TGGGAATAGG AAACAACGGT CGCCAGGCCG
1150 1160 1170 1180 1190 1200
CGGGAACTCA AAGGAGACTG CCAGTGATAA ACTGGAGGAA GGTGGGGATG ACGTCAAGTC
GCCCTTGAGT TTCTCTGAC GGTCACTATT TGACCTCCTT CCACCCCTAC TGCAGTTTAC
ATG ACGTCAAGTC
ATG ACGTCAAGTC

FIG. 88C

SB-1

SB-3
SB-4

1210	1220	1230	1240	1250	1260
ATCATGGCCC TTA					
ATCATGGCCC TTACGA					
ATCATGGCCC TTACGACCCAG	GGCTACACAC	GTGCTACAAT	GGCGCATACA	AAGAGAAGCG	
<u>TAGTACCGGG</u> AATGCTGGTC	CCGATGTGTG	CACGATGTTA	CCGCGTATGT	TTCTCTTCGC	
1270	1280	1290	1300	1310	1320
ACCTCGCGAG	AGCAAGCGGA	CCTCATAAAG	TGCGTCGTAG	TCCGGATTGG	AGTCTGCAAC
TGGAGCGCTC	TCGTTGCGCT	GGAGTATTTC	ACGCAGCATC	AGGCCTAACC	TCAGACGTTG
1330	1340	1350	1360	1370	1380
TCGACTCCAT	GAAGTCGGAA	TCGCTAGTAA	TCGTGGATCA	GAATGCCACG	GTGAATACGT
AGCTGAGGTA	CTTCAGCCTT	AGCGATCATT	AGCACCTAGT	CTTACGGTGC	<u>CACIIATGCA</u>
				GC	CACTTATGCA
1390	1400	1410	1420	1430	1440
TCCCGGGCCT	TGTACACACC	GCCCCGCACA	CCATGGGAGT	GGGTTGCCAA	AGAAGTAGGT
<u>AGGGCCCCGA</u> ACAIGTGTGG	CGGGCAGTGT	GGTACCCTCA	CCCAACGTTT	TCTTCATCCA	
AGGGCCCCGA ACATG					
1450	1460	1470	1480	1490	1500
AGCTTAACCT	TCGGGAGGGC	GCTTACCACCT	TTGTGATTCA	TGACTGGGGT	GAAGTCGTAA
TCGAATTGGA	AGCCCTCCCCG	CGAATGGTGA	AACACTAAGT	ACTGACCCCA	CTTCAGCATT
1510	1520	1530	1540	1550	
CAAGGTAACC	GTAGGGGAAC	CTGCGGTTGG	ATCACCTCCT	TA.....	
GTTCCATTGG	CATCCCCTTG	GACGCCAAC	TAGTGGAGGA	AT.....	

SB-3
SB-4

1743

1743

FIG. 88D



1638 (SEQ ID NO:151) AGAGTTTGATCCTGGCTCAG
E.colirrsE (SEQ ID NO:158)0 ...AAATTGAAGAGTTTGATCATGGCTCAGATTGAACGCTGGCGGCGAGGCCTAACACATGCA
Cam.jejun5 (SEQ ID NO:159)0 ~TTTTTATGGAGAGTTTGATCCTGGCTCAGAGTGAACGCTGGCGGCGTGCCTAATACATGCA
Stp.aureus (SEQ ID NO:160)0 ..TTTTATGGAGAGTTTGATCCTGGCTCAGGATGAACGCTGGCGGCGTGCCTAATACATGCA

ER10 (SEQ ID NO:152)
E.colirrsE GGCGGACGGG
Cam.jejun5 60 AGTCGAACGGTAACAG-----GAAGAAGCTTGCTTCTTT-----GCTGACGAGTGGCGGACGGG
Stp.aureus 62 AGTCGAACGAT-----GAAGCTTCTAGCTTGCTAGAGTGA-----TTAGTGGCGCACGGG
61 AGTCGAGCGAA-----CGGACGAGAAGCTTGCTTCTCTGATG-----TT-AGCGGCGGACGGG

ER10 TGAGTAA
E.colirrsE 114 TGAGTAATGTCTGGGA-AACTGCCTGATGGAGGGGATAACTACTGGAAACGGTAGCTAATA
Cam.jejun5 114 TGAGTAAGGTATAGTTAATCTGCCCTACACAAAGAGGACAACAGTTGGAAACGACTGCTAATA
Stp.aureus 113 TGAGTAACACGCTGGATAACCTACCTATAAGACTGGGATAACTTCGGGAAACCGGAGCTAATA

E.colirrsE 175 CCGCATAAC-----GTCGCAAGAC-----CAAAAGAGGGGACCTTCG-GGCCTCTTG
Cam.jejun5 176 CTCTATACTCCTGCTTAACACAAAGTTGAGTAGG-GAAAG-----TTTTT-----CG
Stp.aureus 175 CCGGATAATATTTTGAACCGCATGGTTCAAAAGTGAAAGACGGT----CTT----GCTGTCA

E.colirrsE 221 CCATCGGATGTGCCAGATGGGATTAGCTAGTGGGTACGGCTCACCTAGGCGACGA
Cam.jejun5 221 GTGTAGGATGAGACTATATAGTATCAGCTAGTTGGTAAGGTAAATGGCTTACCAAGGCTATGA
Stp.aureus 229 CTTATAGATGGATCCGCGCTGCATTAGCTAGTTGGTAAGGTAAACGGCTTACCAAGGCAACGA

E.colirrsE 283 TCCCTAGCTGGTCTGAGAGGATGACCCAGCCACACTGGAACTGAGACACGGTCCAGACTCCTA
Cam.jejun5 283 CGCTTAACCTGGTCTGAGAGGATGATCAGTCACACTGGAACTGAGACACGGTCCAGACTCCTA
Stp.aureus 291 TACGTAGCCGACCTGAGAGGGGTGATCGGCCACACTGGAACTGAGACACGGTCCAGACTCCTA
1659 (COMPL) ACTCCTA

FIG. 89A



E.colirrsE
Cam.jejun5
Stp.aureus
1659 (COMPL)

345 CCGGAGGCAGCAGTGGGGAATATTGCACAAATGGGCGCAAGCCTGATGCAGCCATGCCCGCGTG
345 CCGGAGGCAGCAGTAGGGAAATATTGCGCAATGGGGGAAACCCCTGACGCAGCAACGCCCGCGTG
353 CCGGAGGCAGCAGTAGGGAAATCTTCCGCAATGGGCGAAAGCCTGACGGAGCAACGCCCGCGTG
CGGAGGCAGCAG

E.colirrsE
Cam.jejun5
Stp.aureus

407 TATGAAGAAGGCCTTCGGGTTGTAAAGTACTTTTCAGCGGGGAGGAA-GGGAGTAAAGTTAAT
407 GAGGATGACACTTTTCGGAGCGTAAACTCCTTTCTTAGGGAAAG-----AATT
415 AGTGATGAAGGTCCTTCGGATCGTAAACTCTGTTATTAGGGAAGAACATATGTGTAGTAAC

E.colirrsE
Cam.jejun5
Stp.aureus

468 ACCTTTGCTCATTGACGTTACCCGCAGAAAGCACCGGCTAACTCCGTGCCAGCAGCCCGCG
455 C-----TGACGGTACCTAAGGAAATAAGCACCGGCTAACTCCGTGCCAGCAGCCCGCG
476 -TGTGCACATCTTTGACGGGTACCTAATCAGAAAGCCACGGCTAACTACGTGCCAGCAGCCCGCG

FIG. 89B



<i>E.colirrsE</i>	530	GTAATACGGAGGGTGCAAGCGTTAATCGGAATTACTGGCGCTAAAGCGCACGCGGGGTTT
<i>Cam.jejun5</i>	506	GTAATACGGAGGGTGCAAGCGTTAATCGGAATCACTGGCGCTAAAGGCGCGTAGGCGGATT
<i>Stp.aureus</i>	538	GTAATACGTAGGTGGCAAGCGTTATCCGGAATTATTGGCGCTAAAGCGCGCTAGGCGGTTT
<i>E.colirrsE</i>	592	GTTAAGTCAGATGTGAAATCCCCGGGCTCAACCTGGGAACTGCATCTGATACTGGCAAGCTT
<i>Cam.jejun5</i>	568	ATCAAGTCTCTTGTGAAATCTAATGGCTTAACCATTAACCTGCTTGGGAACTGATAGTCTA
<i>Stp.aureus</i>	600	TTTAAGTCTGATGTGAAAGCCACGGCTCAACCGTGGAGGGTCATTGGAAACTGGAAACTT
<i>E.colirrsE</i>	654	GAGTCTCGTAGAGGGGGTAGAATTCAGGTGTAGCGGTGAAATGCCGTAGAGATCTGGAGGA
<i>Cam.jejun5</i>	630	GAGTGAGGGAGAGGCAGATGGAATTGGTGGTGTAGGGGTAAATCCGTAGATATCACCAAGA
<i>Stp.aureus</i>	662	GAGTGCAGAAAGAGGAAAGTGGAATTCATGTGTAGCGGTGAAATGCCGCAGAGATATGGAGGA
<i>E.colirrsE</i>	716	ATACCGGTGGCGAAGGGGGCCCCCTGGACGAAGACTGACGCTCAGGTGCCGAAAGCGTGGGGA
<i>Cam.jejun5</i>	692	ATACCCATTGCGAAGGCGATCTGCTGGAACCTCAACTGACGCTAAGGCGCGAAAGCGTGGGGA
<i>Stp.aureus</i>	724	ACACCCAGTGGCGAAGGCGACTTCTGTCTGTAACTGACGCTGATGTGCGAAAGCGTGGGGA
<i>E.colirrsE</i>	778	GCAACACAGGATTAGATACCCCTGGTAGTCCACGCGCCGTAAACGATGTCGACTTGGAGGTTGTGC
<i>Cam.jejun5</i>	754	GCAACACAGGATTAGATACCCCTGGTAGTCCACGCGCCGTAAACGATGTACACTAGTTGTTGGGGT
<i>Stp.aureus</i>	786	TCAACACAGGATTAGATACCCCTGGTAGTCCACGCGCCGTAAACGATGAGTGCTAAGTGTTAGGGG

FIG. 89C



E.colirrsE	840	C-CTTGA-GGCGTGGCTTCCGGAGCTAACGCGTTAAGTCGACCGCCTGGGGAGTACGGCCGC
Cam.jejun5	816	G-CTAGT-CATCTCAGTAATGCAGCTAACGCATTAAGTGTAACCGCTGGGGAGTACGGTCGC
Stp.aureus	848	GT-TTCCGCCCCCTTAGTGCTGCAGCTAACGCATTAAGCACTCCGCCTGGGGAGTACGACCGC
E.colirrsE	900	AAGGTTAAACTCAAATGAATTGACGGGGGCCCGCACAAAGCGGTGGAGCATGTGGTTTAATT
Cam.jejun5	876	AAGATTAAACTCAAAGGAATAGACGGGGACCCGCACAAAGCGGTGGAGCATGTGGTTTAATT
Stp.aureus	909	AAGGTTGAAACTCAAAGGAATTGACGGGGACCCGCACAAAGCGGTGGAGCATGTGGTTTAATT
E.colirrsE	962	CGATGCAACGCGAAGAACCTTACCTGGTCTTGACATCCACGGGAAGTTTTTCAGAGATGAGAAT
Cam.jejun5	938	CGAAGATACGCGAAGAACCTTACCTGGCTTGATATCCTAAGAACCTTTTAGAGATAAGAGG
Stp.aureus	971	CGAAGCAACGCGAAGAACCTTACCAAATCTTGACATCCTTTGACAACTCTAGAGATAGAGCC
E.colirrsE	1024	GTG--CCTTCGGG--AA-CCGTGAGACAGGTGCTGCATGGCTCGTCAGCTCGTGTGTGA
Cam.jejun5	1000	GTGCTAGCTTGCTAGAA-CTTAGAGACAGGTGCTGCACGGCTGTCGTCAGCTCGTGTGTGA
Stp.aureus	1033	TTCC-CCTTCGGG--GGACAAAGTGACAGGTGCTGCATGGTTGTCGTCAGCTCGTGTGTGA
SB-1		GCAACGAGCGCAACCC
E.colirrsE	1081	AATGTTGGGTTAAGTCCCGCAACGAGCGCAACCTTATCCTTTGTTGCCAGCGGTCCGG-CC
Cam.jejun5	1061	GATGTTGGGTTAAGTCCCGCAACGAGCGCAACCCACGTAATTTAGTTGCTAACGGTTCGG-CC
Stp.aureus	1092	GATGTTGGGTTAAGTCCCGCAACGAGCGCAACCTTAAGCTTAGTTGCCATCA-TTAAGT-T

FIG. 89D



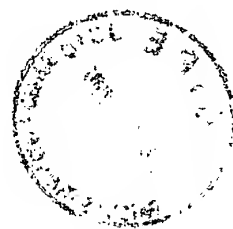
SB-3 (SEQ ID NO:157) ATGACGTCAAGTCATC
 SB-4 (SEQ ID NO:154) ATGACGTCAAGTCATC
 E.colirrsE 1142 GGGAACTCAAAGGAGACTGCCAGTGATAAACTGGAGGAAGGTGGGGATGACGTCAAGTCATC
 Cam.jejun5 1122 GAGCACTCTAAATAGACTGCCCTTCG-TAAGGAGGAGGAAGGTGTGGACGACGTCAAGTCATC
 Stp.aureus 1152 GGGCACTCTAAGTTGACTGCCGGTGACAAACCGGAGGAAGGTGGGGATGACGTCAAAATCATC
 SB-3 ATGGCCCTTA
 SB-4 ATGGCCCTTACGA
 E.colirrsE 1204 ATGGCCCTTACGACCAGGGCTACACACGTGCTACAAATGGCGCATACAAAGAGAGCGACCTC
 Cam.jejun5 1183 ATGGCCCTTATGCCCAGGGCGACACACGTGCTACAATGGCATATAGAAATGAGACGCAATACC
 Stp.aureus 1214 ATGGCCCTTATGATTTGGGCTACACACGTGCTACAAATGGACAATACAAAGGGCAGCGAAACC
 E.colirrsE 1266 GCGAGAGCAAGCGGACCTCATAAAGTGCGTCGTAGTCCGGATTGGAGTCTGCAACTCGACTC
 Cam.jejun5 1245 GCGAGGTGGAG-CAAAATCTATAAAATATGTCCAGTTCGGATTGTTCTCTGCAACTCGAGAG
 Stp.aureus 1276 GCGAGGTCAAGCAAAATCCCATAAAGTTGTTCTCAGTTCGGATTGTAGTCTGCAACTCGACTA
 E.colirrsE 1328 CATGAAGTCGGAATCGCTAGTAATCGTGGATCAGA-ATGCCACGGTGAATACGTTCCCGGGC
 Cam.jejun5 1306 CATGAAGCCGGAATCGCTAGTAATCGTAGATCAGCCATGCTACGGTGAATACGTTCCCGGGT
 Stp.aureus 1338 CATGAAGCTGGAATCGCTAGTAATCGTAGATCAGC-ATGCTACGGTGAATACGTTCCCGGGT
 1743(compl) CGGTGAATACGTTCCCGGGC

FIG. 89E



E.colirrsE 1389 CTTGTACACACCGCCCGTCACACCATGGGAGTGGGTGCAAAAGAAGTAGGTAGCTTAACCT
 Cam.jejun5 1368 CTTGTACTCACC GCCCGTCACACCATGGGAGTTGATTTCACTCGAAGCCGGAATACT--A-A
 Stp.aureus 1399 ATTGTACACACCGCCCGTCACACACCGAGAGTTTGTAAACACCCGAAGCCGGTGGAGTAACCT
 1743(compl) CTTGTAC
 E.colirrsE 1451 TCG-GGAGGGCGCTTACCACCTTTGTGATTTCATGACTGGGGTGAAGTCGTAACAAGGTAACCG
 Cam.jejun5 1427 AC---T-AGTTACCGTCCACAGTGGAATCAGCGACTGGGGTGAAGTCGTAACAAGGTAACCG
 Stp.aureus 1461 TTTAGGAGCTAGCCGTCGAAGGTGGGACAAATGATTGGGGTGAAGTCGTAACAAGGTAAGCCG
 E.colirrsE 1512 TAGGGGAACCTGCGGTTGGATCACCTCCTTA---
 Cam.jejun5 1485 TAGGAGAACCTGCGGTTGGATCACCTCCT-----
 Stp.aureus 1523 TATCGGAAGGTGCGGCTGGATCACCTCCTTTCT-

FIG. 89F



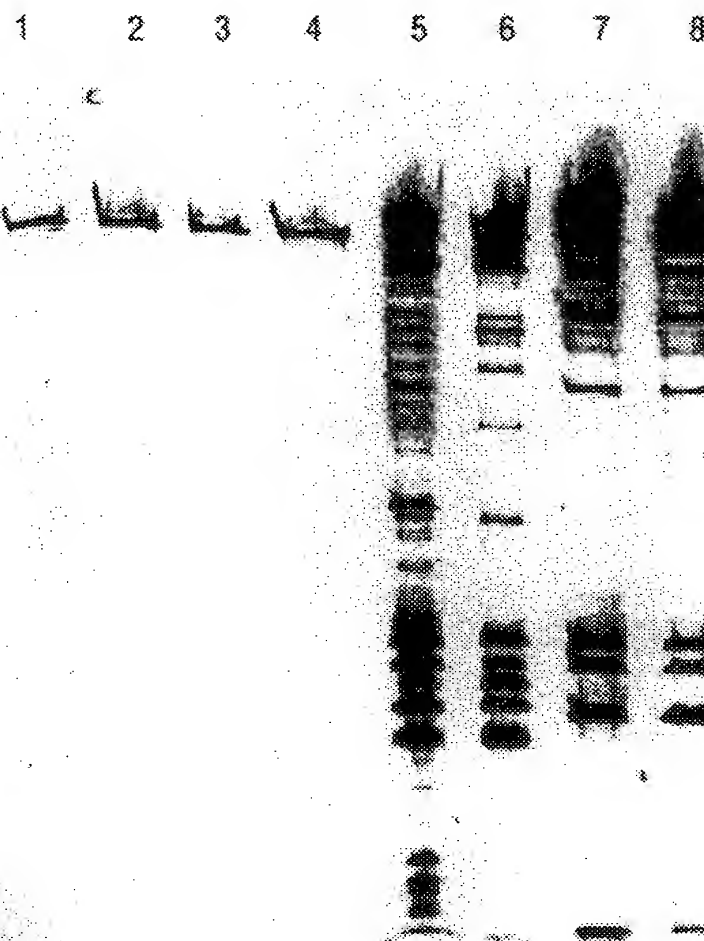


FIG. 90

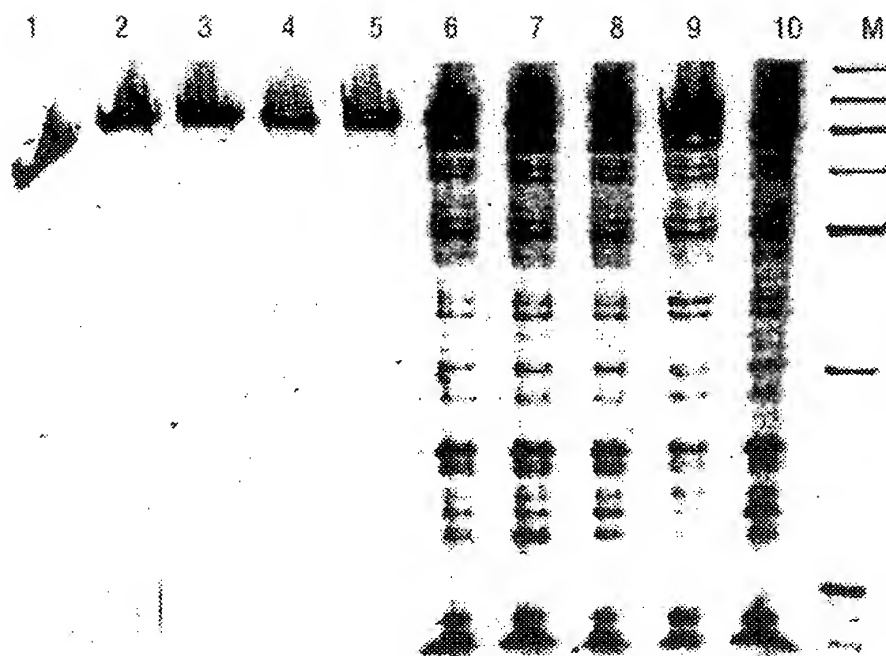


FIG. 91A

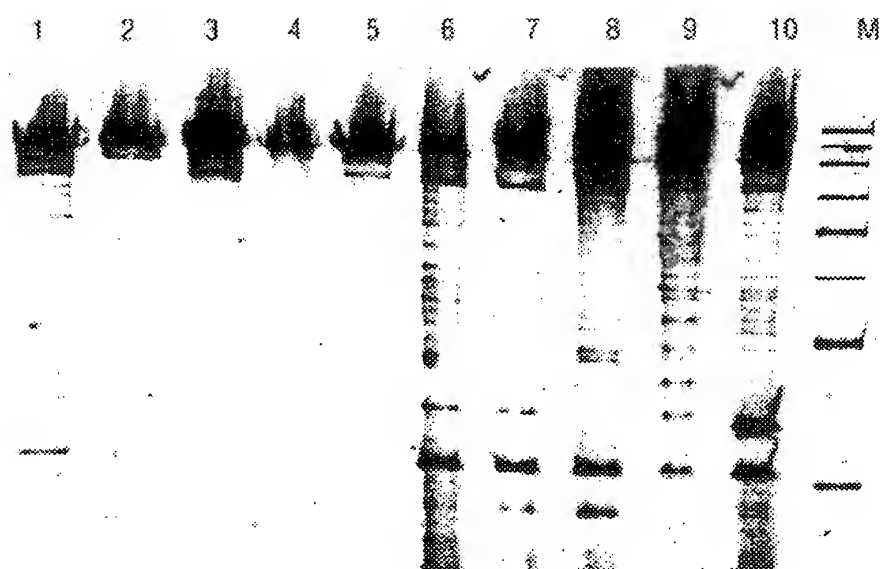
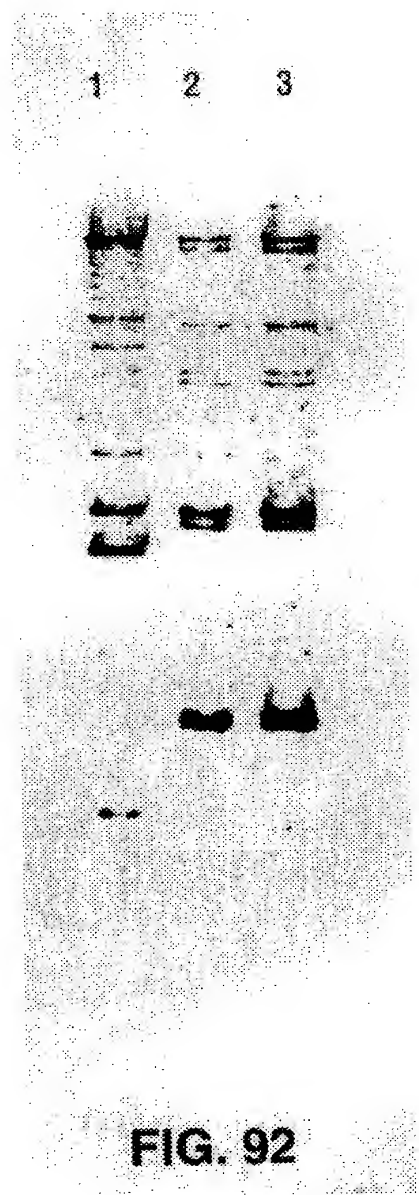


FIG. 91B



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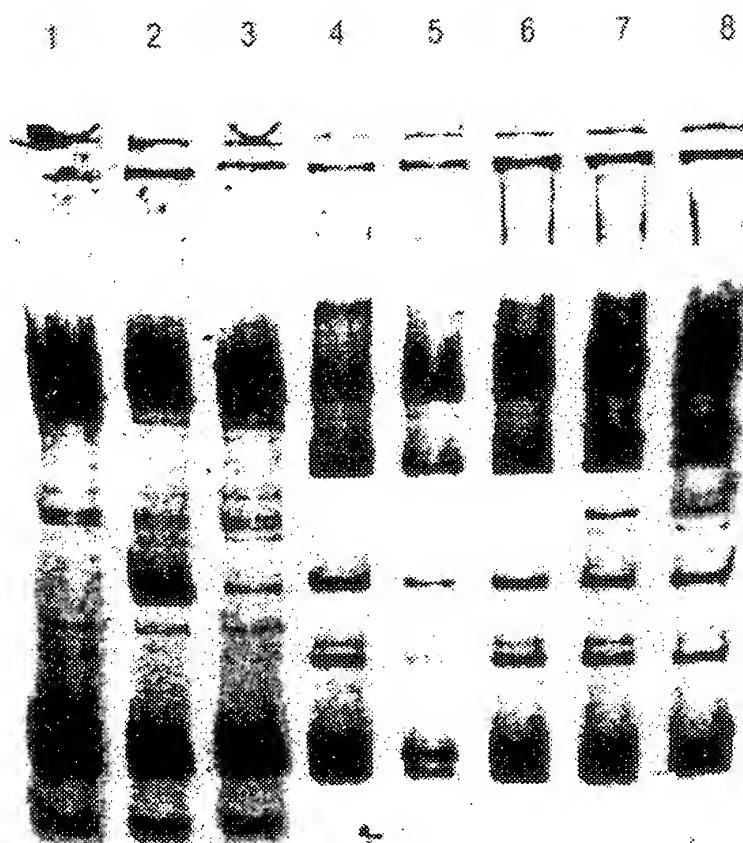


FIG. 93

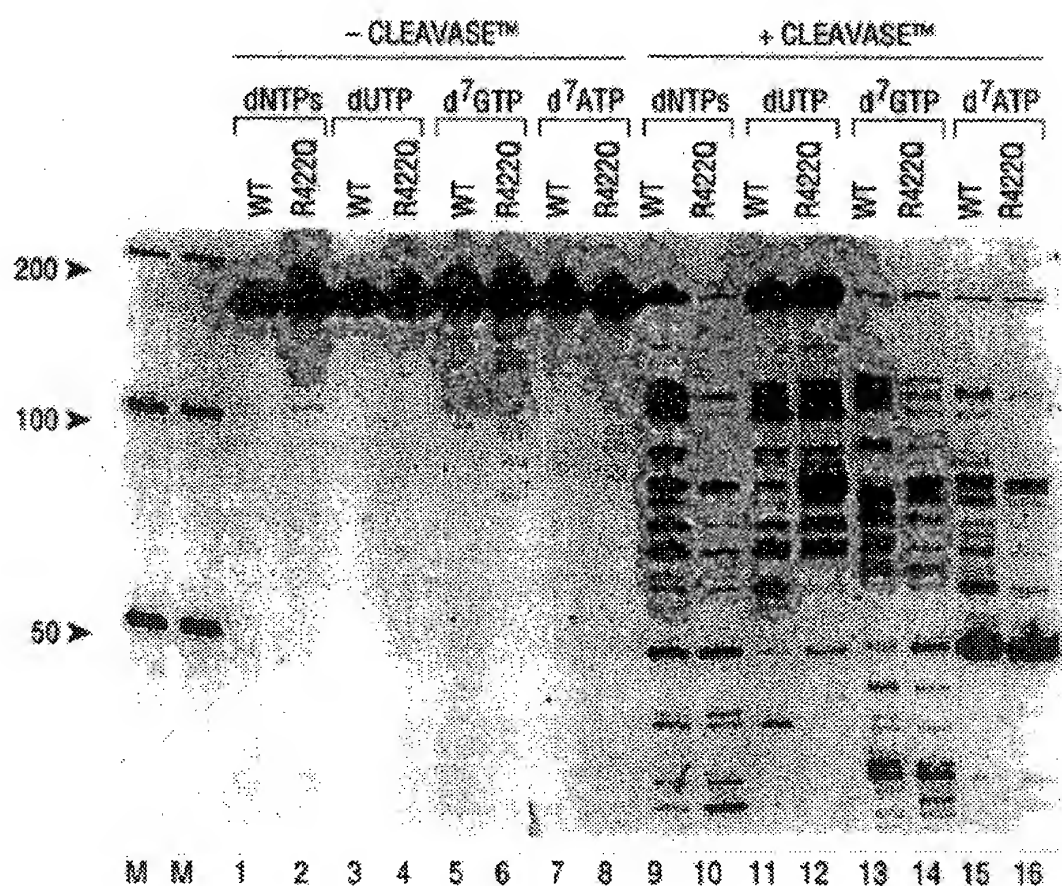


FIG. 94